

## Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID: ssspta1626amd

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* \* \* \* \* \* \* \* \* \* \* Welcome to STN International \* \* \* \* \* \* \* \* \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock  
NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area  
NEWS 4 Apr 09 ZDB will be removed from STN  
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and  
IFIUDB  
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCPLUS, and  
ZCPLUS  
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available  
NEWS 9 Jun 03 New e-mail delivery for search results now available  
NEWS 10 Jun 10 MEDLINE Reload  
NEWS 11 Jun 10 PCTFULL has been reloaded  
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment  
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;  
saved answer sets no longer valid  
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY  
NEWS 15 Jul 30 NETFIRST to be removed from STN  
NEWS 16 Aug 08 CANCERLIT reload  
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 18 Aug 08 NTIS has been reloaded and enhanced  
NEWS 19 Aug 09 JAPIO to be reloaded August 25, 2002  
NEWS 20 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
NEWS 21 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded  
NEWS 22 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002

NEWS HOURS STN Operating Hours Plus Help Desk Availability

NEWS INTER General Internet Information

NEWS LOGIN Welcome Banner and News Items

NEWS PHONE Direct Dial and Telecommunication Network Access to STN

NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* \* \* \* \* \* \* \* \* \* \* STN Columbus \* \* \* \* \* \* \* \* \* \* \* \* \* \* \*

FILE 'HOME' ENTERED AT 13:21:47 ON 20 AUG 2002

=> fil reg		SINCE FILE	TOTAL
COST IN U.S. DOLLARS		ENTRY	SESSION
FULL ESTIMATED COST		0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:21:54 ON 20 AUG 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5  
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

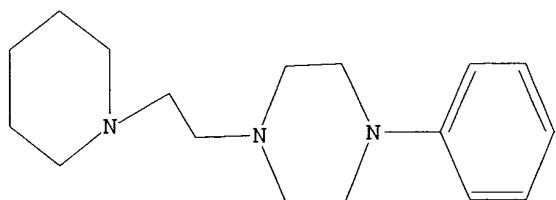
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>  
Uploading 09764710.str

L1 STRUCTURE uploaded

=> d  
L1 HAS NO ANSWERS  
L1 STR



Structure attributes must be viewed using STN Express query preparation.

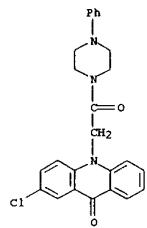
=> s l1 ful  
FULL SEARCH INITIATED 13:22:10 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 6501 TO ITERATE

100.0% PROCESSED 6501 ITERATIONS  
SEARCH TIME: 00.00.01

317 ANSWERS

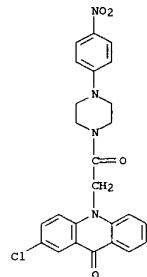
L2 317 SEA SSS FUL L1  
=> s l2 and caplus/lc  
23929408 CAPLUS/LC  
L3 288 L2 AND CAPLUS/LC  
=> s l2 not l3  
L4 29 L2 NOT L3  
=> d 1-29

L4 ANSWER 1 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 420834-76-0 REGISTRY  
CN Piperazine, 1-[(2-chloro-9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl-(9CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C25 H22 Cl N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



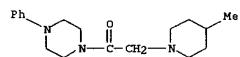
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 2 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 403716-00-7 REGISTRY  
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FS 3D CONCORD  
MF C25 H21 Cl N4 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



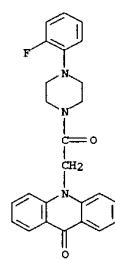
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 3 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 397880-89-6 REGISTRY  
CN Piperazine, 1-[(4-methyl-1-piperidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C18 H27 N3 O  
SR Chemical Library  
LC STN Files: CHEMCATS



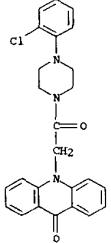
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 4 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 389577-94-0 REGISTRY  
CN Piperazine, 1-(2-fluorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C25 H22 F N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



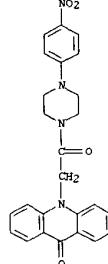
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 5 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 389577-90-6 REGISTRY  
CN Piperazine, 1-(2-chlorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-  
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(CA INDEX NAME)  
FS 3D CONCORD  
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SR Chemical Library  
LC STN Files: CHEMCATS



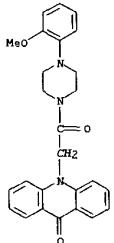
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 6 OF 29 REGISTRY COPYRIGHT 2002 ACS  
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SR Chemical Library  
LC STN Files: CHEMCATS



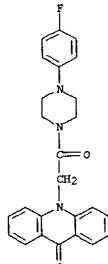
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 7 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 389577-87-1 REGISTRY  
CN Piperazine, 1-(2-methoxyphenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-  
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SR Chemical Library  
LC STN Files: CHEMCATS



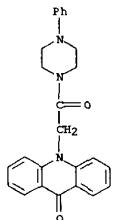
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 8 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 389577-29-1 REGISTRY  
CN Piperazine, 1-(4-fluorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-  
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(CA INDEX NAME)  
FS 3D CONCORD  
MF C25 H22 F N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



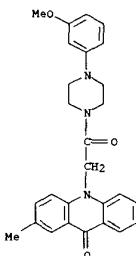
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 9 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 389577-27-9 REGISTRY  
CN Piperazine, 1-[ (9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)  
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FS 3D CONCORD  
MF C25 H23 N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



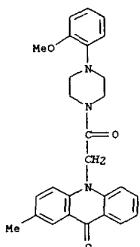
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 10 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 362494-03-9 REGISTRY  
CN Piperazine, 1-(3-methoxyphenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C27 H27 N3 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



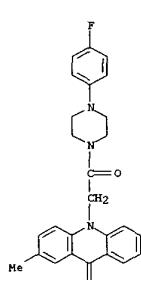
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 11 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 362493-98-9 REGISTRY  
CN Piperazine, 1-(2-methoxyphenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)  
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SR Chemical Library  
LC STN Files: CHEMCATS



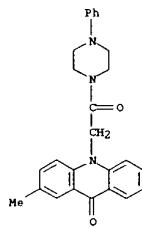
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 12 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 362493-85-4 REGISTRY  
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FS 3D CONCORD  
MF C26 H24 F N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



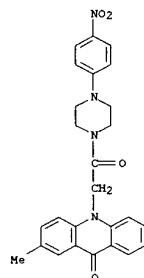
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 13 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 362493-56-9 REGISTRY  
CN Piperazine, 1-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl-  
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(CA INDEX NAME)  
FS 3D CONCORD  
MF C26 H25 N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



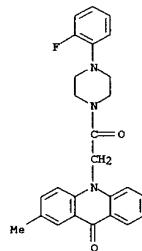
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 14 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 362493-55-8 REGISTRY  
CN Piperazine,  
1-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-4-(4-nitrophenyl)-  
(9CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C26 H24 N4 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



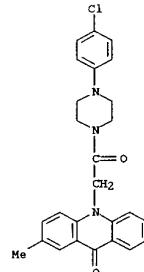
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 15 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 362493-49-0 REGISTRY  
CN Piperazine,  
1-(2-fluorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-  
(9CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C26 H24 F N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



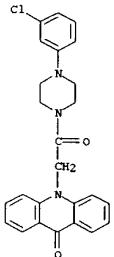
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 16 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 361197-24-2 REGISTRY  
CN Piperazine,  
1-(4-chlorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-  
(9CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C26 H24 Cl N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS

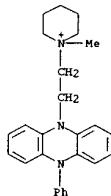


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 17 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 361188-24-1 REGISTRY  
CN Piperazine, 1-(3-chlorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-  
(SCI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C25 H22 Cl N3 O2  
SR Chemical Library  
LC STN Files: CHEMCATS

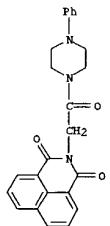


L4 ANSWER 18 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 342603-26-3 REGISTRY  
CN Piperidinium, 1-methyl-1-[2-(10-phenyl-5(10H)-phenazinyl)ethyl]- (9CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C26 H30 N3  
CI COM  
SR CA



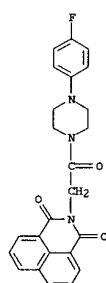
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 19 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 326889-78-5 REGISTRY  
CN Piperazine, 1-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)acetyl]-4-phenyl-  
(SCI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H21 N3 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 20 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 326889-59-2 REGISTRY  
CN Piperazine,  
1-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)acetyl]-4-(4-  
fluorophenyl)- (SCI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H20 F N3 O3  
SR Chemical Library  
LC STN Files: CHEMCATS

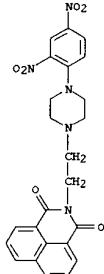
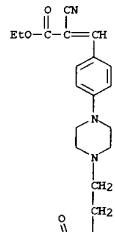


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 21 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 324774-78-9 REGISTRY  
CN 2-Propenoic acid,  
2-cyano-3-[4-[2-(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)ethyl]-1-piperazinyl]phenyl-, ethyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C30 H28 N4 O4  
SR Chemical Library  
LC STN Files: CHEMCATS

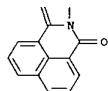
L4 ANSWER 22 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 309735-93-1 REGISTRY  
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-{4-(2,4-dinitrophenyl)-1-piperazinyl}ethyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H21 N5 O6  
SR Chemical Library  
LC STN Files: CHEMCATS

PAGE 1-A



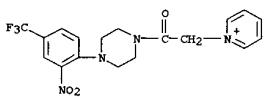
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

PAGE 2-A



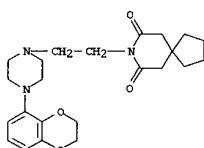
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 23 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 219139-24-9 REGISTRY  
CN Pyridinium,  
1-[2-[4-[2-nitro-4-(trifluoromethyl)phenyl]-1-piperazinyl]-2-oxoethyl]-, chloride (9CI) (CA INDEX NAME)  
MF C18 H18 F3 N4 O3 Cl  
SR CAS Registry Services  
LC STN Files: CHEMCATS



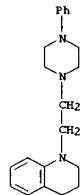
● Cl<sup>-</sup>

L4 ANSWER 24 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 171877-12-6 REGISTRY  
CN 8-Azaspiro[4.5]decane-7,9-dione,  
8-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H31 N3 O4  
CI COM  
SR CA



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

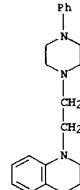
L4 ANSWER 25 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 112991-17-0 REGISTRY  
CN Quinoline, 1,2,3,4-tetrahydro-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride (6CI) (CA INDEX NAME)  
MF C21 H27 N3 . Cl H  
SR CAOLD  
LC STN Files: CAOLD  
CRN (110081-34-0)



● HCl

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 26 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 110081-34-0 REGISTRY  
CN Quinoline, 1,2,3,4-tetrahydro-1-[2-(4-phenyl-1-piperazinyl)ethyl]- (6CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H27 N3  
CI COM  
SR CAOLD  
LC STN Files: BEILSTEIN\*, CAOLD  
(\*File contains numerically searchable property data)

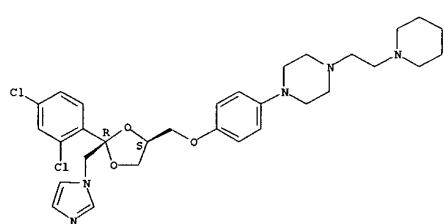


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

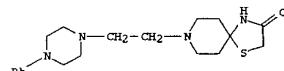
L4 ANSWER 27 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 75049-52-4 REGISTRY  
CN Piperazine,  
1-[4-[(2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl)methoxy]phenyl]-4-(2-(1-piperidinyl)ethyl)-, cis- (9CI) (CA INDEX NAME)  
PS STEREOSEARCH  
MF C31 H39 Cl2 N5 O3  
CI COM

Relative stereochemistry.



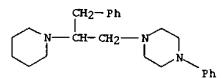
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 28 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 54950-44-6 REGISTRY  
CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one,  
8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H28 N4 O S  
CI COM



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 ANSWER 29 OF 29 REGISTRY COPYRIGHT 2002 ACS  
RN 7029-67-6 REGISTRY  
CN Piperazine, 1-phenyl-4-(3-phenyl-2-piperidinopropyl)- (7CI, 8CI) (CA  
INDEX NAME)  
FS 3D CONCORD  
MF C24 H33 N3  
LC STN Files: BEILSTEIN\*, CAOLD  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> fil caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST
```

	SINCE FILE	TOTAL
	ENTRY	SESSION
	190.48	190.69

FILE 'CAPLUS' ENTERED AT 13:22:49 ON 20 AUG 2002  
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8  
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d his

(FILE 'HOME' ENTERED AT 13:21:47 ON 20 AUG 2002)

FILE 'REGISTRY' ENTERED AT 13:21:54 ON 20 AUG 2002

L1           STRUCTURE uploaded
L2           317 S L1 FUL
L3           288 S L2 AND CAPLUS/LC
L4           29 S L2 NOT L3

FILE 'CAPLUS' ENTERED AT 13:22:49 ON 20 AUG 2002

=> s 13
L5         211 L3

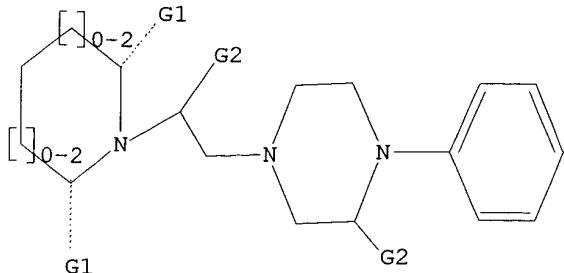
=>
Uploading 09764710.str

L6         STRUCTURE uploaded

=> s
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):end

SEARCH ENDED BY USER

=> d  
L6 HAS NO ANSWERS  
L6 STR



G1 H,O,S  
G2 H,Ak

Structure attributes must be viewed using STN Express query preparation.

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.77	193.46

FILE 'REGISTRY' ENTERED AT 13:26:55 ON 20 AUG 2002  
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STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5  
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s 16 subset=l2 ful  
FULL SUBSET SEARCH INITIATED 13:27:08 FILE 'REGISTRY'  
FULL SUBSET SCREEN SEARCH COMPLETED - 317 TO ITERATE

100.0% PROCESSED 317 ITERATIONS  
SEARCH TIME: 00.00.01

265 ANSWERS

L7 265 SEA SUB=L2 SSS FUL L6

=> s 17 not 12  
L8 0 L7 NOT L2

=> s 17 and caplus/lc  
23929408 CAPLUS/LC  
L9 255 L7 AND CAPLUS/LC

=> fil caplus  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 37.43 230.89

FILE 'CAPLUS' ENTERED AT 13:27:34 ON 20 AUG 2002  
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8  
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s 19  
L10 194 L9

=> fil reg  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 0.40 231.29

FILE 'REGISTRY' ENTERED AT 13:27:59 ON 20 AUG 2002  
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STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5  
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

```
=> s 17 ful
FULL SEARCH INITIATED 13:28:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6498 TO ITERATE
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```
100.0% PROCESSED      6498 ITERATIONS          481 ANSWERS
SEARCH TIME: 00.00.01
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L11 481 SEA SSS FUL L6

```
=> s l11 and caplus/lc
      23929408 CAPLUS/LC
L12      444 L11 AND CAPLUS/LC
```

```
=> fil caplus
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                               ENTRY           SESSION
FULL ESTIMATED COST          144.66          375.95
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```
FILE 'CAPLUS' ENTERED AT 13:28:54 ON 20 AUG 2002
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> s l12  
L13      263 L12
```

```
=> fil caplus  
COST IN U.S. DOLLARS          SINCE FILE      TOTAL  
                               ENTRY SESSION  
FULL ESTIMATED COST          0.40    376.35
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FILE 'CAPLUS' ENTERED AT 13:29:27 ON 20 AUG 2002  
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8  
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

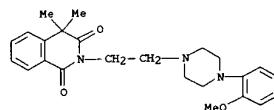
CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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=> s l13  
L14      263 L12  
  
=> d 1-263 ibib abs hitstr
```

L14 ANSWER 1 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:521523 CAPLUS  
 DOCUMENT NUMBER: 137:73273  
 TITLE: Adrenergic receptor ligand-neurotoxin conjugates  
 and  
 methods for treating pain  
 INVENTOR(S): Gil, Daniel W.; Aoki, Kei Roger  
 PATENT ASSIGNEE(S): Allergan Sales, Inc., USA  
 SOURCE: PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053177	A2	20020711	WO 2001-US48651	20011214
		W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
PRIORITY APPLN. INFO.:			US 2000-751053	A 200001229
OTHER SOURCE(S):			MARPAT 137:73273	
AB	Agents for treating pain, methods for producing the agents, and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent, are disclosed. The agent may include a clostridial neurotoxin, a fragment or a deriv. thereof, attached to a targeting component, wherein the targeting component is selected from a group consisting of compds. which selectively binds at the .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptor subtype(s) as compared to other binding sites, e.g. the .alpha.2a adrenergic receptor subtype.			
IT	67339-62-2D, ARC 239, conjugates RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain)			
RN	67339-62-2 CAPLUS			
CN	1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1- piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)			

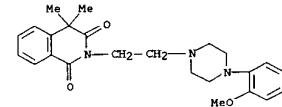
L14 ANSWER 1 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 2 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:408903 CAPLUS  
 DOCUMENT NUMBER: 136:395968  
 TITLE: Remedies for digestive functional disorder and  
screening method  
 INVENTOR(S): Yamamoto, Osamu  
 PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 19 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042765	A1	20020530	WO 2001-JP10152	20011121
		W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
PRIORITY APPLN. INFO.:			JP 2000-356040	A 20000122
AB	Medicinal compns. contg. as the active ingredient an adrenergic .alpha.2B receptor selective antagonist, an adrenergic .alpha.2C receptor selective antagonist or an adrenergic .alpha.2B/2C receptor selective antagonist; and a method of screening the same. Namely, medicinal compns. for treating irritable bowel syndrome which have an excellent effect of improving enteric movement and high safety; and a method useful in screening the same.			
IT	67339-62-2, ARC239 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adrenergic .alpha.2 B and C antagonists as remedies for digestive functional disorder and screening method)			
RN	67339-62-2 CAPLUS			
CN	1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1- piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)			

L14 ANSWER 2 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 3 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:392232 CAPLUS  
 DOCUMENT NUMBER: 136:401912  
 TITLE: Nitrosated and nitrosylated alpha-adrenergic receptor antagonist compounds, compositions and their uses  
 INVENTOR(S): Garvey, David S.; Schroeder, Joseph D.; Saenz de Tejada, Inigo  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S.  
 Ser. No. 714,313.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061879	A1	20020523	US 2001-24550	20011221
US 5932538	A	19990803	US 1996-595732	19960202
US 5994294	A	19991130	US 1996-714313	19960918
PRIORITY APPLN. INFO.:		US 1996-595732	A2	19960202
		US 1996-714313	A2	19960918

OTHER SOURCE(S): MARPAT 136:401912  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The present invention is directed to nitrosated or nitrosylated a-adrenergic receptor antagonists, e.g. I [Ra = H, alkoxy; Rb = NMe(CH2)2NHCO2C, 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl; a=2, 3; Rc = heteroaryl, heterocycle, lower alkyl, hydroxylalkyl, arylheterocycle; D = NO, NO2, C(Rd)OC(O)YZ(CReRf)pTQ; Rd = H, lower alkyl, cycloalkyl, aryl aralkyl, heterocyl; Y = O, S, C, NR1; Ri = H, lower alkyl; Re, Rf = H, lower alkyl, haloalkyl, cycloalkyl, alkoxy, aryl, heterocyl, NH2, (di)alkylamino, amido, CO2H, ester, TQ; ReRf = carbonyl, heterocycle, cycloalkyl; p = 1 - 10; T = bond, O, S, N; Z = bond, lower alkyl, haloalkyl, cycloalkyl, aryl, (CReRf)p, Q = NO, NO2], II [R = CH2(C6H4Me-4)-C(=O)CH2OD1-3, CH2Ph, 2-methoxy-1,4-benzodioxin-2-yl, 1-methyl-1,2,3-dihydroisoindol-2-yl, 5-chloro-2,3-dihydroisoindol-2-yl; D1 = H, D], III [Rh = H, C(O)ORD, C(O)X; X = Y(CReRf)p(CReRf)pTQ; G = bond, TC(O), C(O)T, C(YC(O)Rm); Rm = heteroaryl, heterocycle], IV [A1 = O, CH2], V, (RmRkC)N(D1)(CRkRl) (Rk = H, lower alkyl; Rl = CH2C6H4O(CH2)bMe, CH2C6H4OD, CH2C6H3(OMe)2-2,6, CH2CH2Ph; b = 0, 1; Rn = CH2C6H4(SO2NH2)-3,

L14 ANSWER 3 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 1-exotetralin-2-yl, 1,4-benzodioxin-2-yl] and RP&gt;C(=O)(Ro)OD [Ro = (1-naphthoxy)methyl, C6H4OD1; Rp = 4-benzylpiperidino, 4-(2-methoxyphenyl)piperazinol]. The present invention is also directed to compns. comprising a, alpha,-adrenergic receptor antagonists that are optionally substituted with at least one NO or NO2 moiety and compds.

that donate, transfer or release nitric oxide or elevate levels of endogenous endothelium-derived relaxing factor, and methods for treating sexual dysfunctions in males and females. Thus, 5-Nitroso-glutathione was prep.

from glutathione via reaction with NaNO2 in aq. HCl.

S-Nitroso-glutathione at 50 mg was able to induce near maximal erectile response in anesthetized rabbits.

IT 67339-62-2, ANC 239, nitrosated or nitrosylated

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

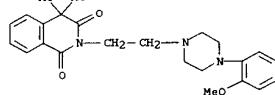
(prep. of nitrosated and nitrosylated alpha-adrenergic receptor

antagonist compds., compns. and their uses)

RN 67339-62-2 CAPLUS

CN 1,3(2H,4H)-1-isquinalinedione, 2-[2-[4-(2-methoxyphenyl)-1-

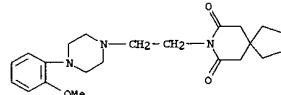
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 4 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:368310 CAPLUS  
 DOCUMENT NUMBER: 136:363866  
 TITLE: Serotonergic compositions and methods for treatment of mild cognitive impairment  
 INVENTOR(S): Wurtman, Richard J.; Lee, Robert K. K.  
 PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA  
 SOURCE: PCT Int. Appl., 34 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038142	A2	20020516	WO 2001-US43016	20011108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-246615P	F 20001108
AB A method of treating mild cognitive impairment is disclosed. The method comprises administering an effective amt. of serotonergic agent, including, but not limited to, dextrofenfluramine. The agent can be any serotonergic agonist, partial agonist, serotonin reuptake inhibitor, or combinations of these agents. The treatment method also encompasses combinations of serotonergic agents and nonsteroidal antiinflammatory agents. The treatment method may also delay the onset of mild cognitive impairment, dementia, or both.				
IT 21102-93-4, EMY 7378				
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(serotonergic compns. and methods for treatment of mild cognitive impairment)				
RN 21102-93-4 CAPLUS				
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-				
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)				

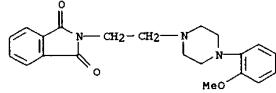
L14 ANSWER 4 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



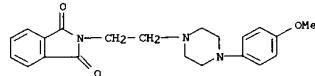
●2 HCl

L14 ANSWER 5 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:314042 CAPLUS  
 DOCUMENT NUMBER: 137:78925  
 TITLE: Design, synthesis and biological activity study  
 on amide series as  $\alpha$ .1-adrenoceptor antagonists  
 AUTHOR(S): Fang, Hao; Xia, Lin; Jiang, Zhen-Zhou; Zhang, Wei;  
 Zhang, Liu-Yong  
 CORPORATE SOURCE: Department of Medicinal Chemistry, China  
 Pharmaceutical University, Nanjing, 210009, Peop. Rep.  
 SOURCE: China  
 Huaxue Xuebao (2002), 60(4), 725-731  
 PUBLISHER: CODEN: HHHPA4; ISSN: 0567-7351  
 DOCUMENT TYPE: Kexue Chubanshe  
 LANGUAGE: Journal  
 OTHER SOURCE(S): Chinese  
 137:78925  
 AB Novel furan-2-carboxylic acid ( $\omega$ -omega.-[4-(substituted phenyl)-piperazine-1-yl]alkyl)amide and 2-oxo-2H-chromene-3-carboxylic acid ( $\omega$ -omega.-[4-(substituted phenyl)piperazine-1-yl]alkyl)amide derivs. have been designed and synthesized based on the structure and activity relationship (SAR) of phenylpiperazine series as  $\alpha$ .1-adrenoceptor ( $\alpha$ .1-AR) antagonists and the results of computer-aided drug design we studied before. All the target compds. have been identified by 1H NMR, IR and MS (HRMS). Preliminary bioassay suggests that most of the target compds. display good blocking activity to  $\alpha$ .1-AR. The potency (pA2) of compd. N-(2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl)-2-furancarboxamide is higher than prazosin.  
 IT 99718-67-9P 117046-73-8P 440117-82-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (synthesis and biol. activity of phenylpiperazinylalkyl amides as  $\alpha$ .1-adrenoceptor antagonists)  
 RN 99718-67-9 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-  
 (9CI) (CA INDEX NAME)

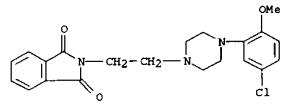
L14 ANSWER 5 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



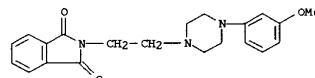
RN 117046-73-8 CAPLUS  
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 (9CI) (CA INDEX NAME)



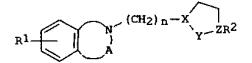
RN 440117-82-8 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-  
 (9CI) (CA INDEX NAME)



RN 440117-88-4 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-  
 (9CI) (CA INDEX NAME)

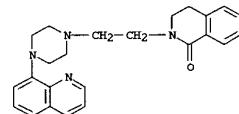


L14 ANSWER 6 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:31419 CAPLUS  
 DOCUMENT NUMBER: 136:85830  
 TITLE: Preparation of bicyclic lactams and sulfonamides as 5-HT1A agonists  
 INVENTOR(S): Steiner, Gerd; Schellhaas, Kurt; Szabo, Laszlo; Behl, Berthold; Garcia-Ladona, Francisco Javier; Unger, Liliane  
 PATENT ASSIGNEE(S): Knoll GmbH, Germany  
 SOURCE: PCT Int. Appl., 39 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 WO 2002002529 A1 20020110 WO 2001-EP7571 20010702  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,  
 CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,  
 GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
 LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,  
 PT,  
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
 US,  
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SI, SZ, TZ, UG, ZW, AT, BE, CH,  
 CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 DE 10031391 A1 20020207 DE 2000-10031391 20000703  
 PRIORITY APPLN. INFO.: DE 2000-10031391 A 20000703  
 OTHER SOURCE(S): MARPAT 136:85830  
 GI



AB Title compds. [I]: the ring including NA can be a 5-7 membered ring contg. O, S, or double bond; A = CO, SO2; X = N; Y = CH2, CH2CH2, (CH2)3, CH2CH2; Z = N, C; CH2 n = 2-4; R1 = H, halo, alkyl, CF3, OH, alkoxy, amino; R2 =

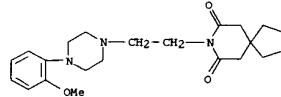
L14 ANSWER 6 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (substituted) (annelated) Ph, pyridyl, pyrazinyl and salts thereof, were  
 prep'd. Thus, isoquinoline in DMF was stirred with NaH for 30 min. followed by addn. of 1-[4-(2-chloroethyl)-1-piperazinylisoquinoline (prepn. given) and stirring for 2 h at 80.degree. to give 82% 2-[2-(4-(1-isoquinoliny)-1-piperazinyl)ethyl]-1(2H)-isoquinoline.2HCl.2H2O. Tested I showed affinity for the 5-HT1A receptor with Ki = 0.1-5.4 nM in HEK 293 cells.  
 IT 387399-38-4P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of bicyclic lactams and sulfonamides as 5-HT1A agonists)  
 RN 387399-38-4 CAPLUS  
 CN 1(2H)-Isoquinolinone, 3,4-dihydro-2-[2-[4-(8-quinolinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:2436 CAPLUS  
 DOCUMENT NUMBER: 136:226674  
 TITLE: A-315456: a selective .alpha.1D-adrenoceptor antagonist with minimal dopamine D2 and 5-HT1A receptor affinity  
 AUTHOR(S): Buckner, Steven A.; Milicic, Ivana; Daza, Anthony; Lynch, James J.; Kolas, Teodozja; Nakane, Masaki;  
 CORPORATE SOURCE: Sullivan, James P.; Brioni, Jorge D.  
 SOURCE: Abbott Laboratories, Abbott Park, IL,  
 European Journal of Pharmacology (2001), 433(1), 123-127  
 CODEN: EUPHAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In functional assays, A-315456, N-[3-(cyclohexylidene-1H-imidazol-4-ylmethyl)phenyl]ethanesulfonamide, behaved as an .alpha.1D-adrenoceptor subtype selective antagonist ( $pA_2=8.34$ ) in the rat aorta. It was 83-fold less potent at the .alpha.1B-adrenoceptor subtype expressed in the rat spleen, and was inactive at the .alpha.1A-adrenoceptor subtype expressed in the rat vas deferens. Radioligand binding assays also revealed high affinity ( $pKi=8.71$ ) for the .alpha.1D-adrenoceptor subtype and weaker affinities at the .alpha.1A-adrenoceptor ( $pKi=6.23$ ) and .alpha.1B-adrenoceptor ( $pKi=7.86$ ). In comparison to its potent affinity at the .alpha.1D-adrenoceptor subtype, A-315456 was 3020-, 794- and 38-fold weaker at the dopamine D2-, 5-HT1A-, and .alpha.2A-adrenoceptors, resp. These studies indicate that A-315456 is a potent and selective .alpha.1D-antagonist that may serve as a useful pharmacol. ligand to probe the physiol. role of the .alpha.1D-adrenoceptor subtype in normal and disease states.  
 IT 21102-95-4, BMY-7378 255893-38-0, SNAP 8719  
 RL: PAC (Pharmacological activity); BIOL (Biological study)  
 (A-315456, a selective .alpha.1D-adrenoceptor antagonist with minimal dopamine D2 and 5-HT1A receptor affinity)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

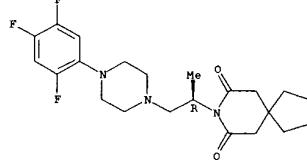
L14 ANSWER 7 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

RN 255893-38-0 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[{(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

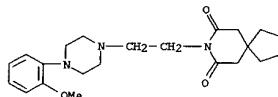


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L14 ANSWER 8 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:78964 CAPLUS  
 DOCUMENT NUMBER: 136:64512  
 TITLE: Functional characterization of .alpha.1-adrenoceptor subtypes in human subcutaneous resistance arteries  
 AUTHOR(S): Jarajapu, Yagna P.R.; Johnston, Fiona; Berry, Colini; Renwick, Andrew; McGrath, John C.; MacDonald, Allan; Hillier, Chris  
 CORPORATE SOURCE: Vascular Assessment Unit, School of Biological and Biomedical Sciences, Glasgow Caledonian University, Glasgow, UK  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 298(2), 729-734  
 CODEN: JPETAB; ISSN: 0022-3565  
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The functional characteristics of the .alpha.1-adrenoceptor subtypes in human resistance arteries are still not clear. The authors recently reported that the .alpha.1A-adrenoceptor predominantly mediates contraction to norepinephrine in human skeletal muscle resistance arteries. In this study the authors extended these investigations to human s.c. resistance arteries. Arterial segments were isolated from the inguinal s.c. fat and mounted on a small vessel wire myograph. Potencies of agonists and antagonists were examined. N-[5-(4,5-dihydro-1H-imidazol-2-yl)-2-hydroxy-5,6,7,8-tetrahydronaphthalen-1-yl]methanesulfonamide (A-61603) was found to be 10- and 54-fold more potent than norepinephrine and phenylephrine, resp. Brimonidine (UK 14304) evoked significantly smaller contractile responses than norepinephrine and phenylephrine, showing the presence of a small population of .alpha.2-adrenoceptors in these arteries, and this was confirmed by the studies with selective .alpha.1- and .alpha.2-adrenoceptor antagonists prazosin and (8aR, 12aS)-13aS-5,8,8a,9,10,11,12,12a,13a-decahydro-3-methoxyl-12-(ethylsulfonyl)-6H-isooquinol[2,1-g][1,6]-naphthyridine (RS 79948). Prazosin, 5-methyl-urapidil, and 2-[2,6-dimethoxyphenyl]aminomethyl-1,4-benzodioxane (WB 4101) shifted the potency of norepinephrine concentration-dependently giving  $pA_2$  values of 9.4, 8.9, and 10.1, resp., showing the presence of the .alpha.1A-subtype in these arteries. Pretreatment with

L14 ANSWER 8 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 max. and 10 .mu.M chloroethylclonidine did not affect the potency of and max. responses to norepinephrine, ruling out the presence of the .alpha.1B-subtype in these arteries. 8-[2-(4-(2-Methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4,5]decane-7,9-dione (BMY 7378, 10 and 100 nM) did not affect the potency of norepinephrine but a small shift was observed by 1 .mu.M BMY 7378, giving a  $pK_B$  value of 7.1, much less than that reported for the .alpha.1D-subtype. These results suggest the predominant involvement of .alpha.1A-adrenoceptor in the contractile responses to norepinephrine in these arteries. The physiol. role of this subtype in the maintenance of peripheral arterial resistance is yet to be confirmed.  
 IT 21102-95-4, BMY 7378  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (pharmacol. characterization of .alpha.1-adrenoceptor subtypes in human s.c. resistance arteries)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L14 ANSWER 9 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:781185 CAPLUS  
 DOCUMENT NUMBER: 135:328176  
 TITLE: Polymorphisms in human .alpha.2 adrenergic receptor genes and their diagnostic and therapeutic uses  
 INVENTOR(S): Liggett, Stephen B.; Small, Kirsten M.  
 PATENT ASSIGNEE(S): US  
 SOURCE: PCT Int. Appl., 163 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079561	A2	20011025	WO 2001-US12575	20010417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, US, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPN. INFO.:			US 2000-551744	A 20000417
			US 2000-636259	A 20000810
			US 2000-692077	A 20001019

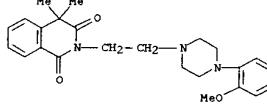
AB The present invention includes polymorphisms in nucleic acids encoding the .alpha.2B, .alpha.2A, and .alpha.2C adrenergic receptor genes and expressed .alpha.2B, .alpha.2A and .alpha.2C adrenergic receptor protein mol. The invention also pertains to methods and mols. for detecting such polymorphisms. The invention further pertains to the use of such mols. and methods in the diagnosis and treatment of diseases such as cardiovascular and central nervous system disease. Genetic polymorphisms of deletion/insertions and single nucleotides in the intracellular loop 3 region of human .alpha.2 adrenergic receptors were identified and characterized to search for correlations between the polymorphisms and physiol. signaling functions of the receptors. Recombinant polymorphic receptor proteins were expressed in cell lines to measure ligand binding,

L14 ANSWER 10 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:776249 CAPLUS  
 DOCUMENT NUMBER: 137:433  
 TITLE: The hypotensive effect of EMY 7378 is antagonized by a silent 5-HT1A receptor antagonist: Comparison with 8-hydroxy-dipropylamino tetralin  
 AUTHOR(S): Villalobos-Molina, Rafael; Lopez-Guerrero, J. Javier;  
 CORPORATE SOURCE: Ibarra, Maximiliano  
 Departamento de Farmacobiología, Centro de Investigación y de Estudios Avanzados (CINVESTAV), Instituto Politécnico Nacional (IPN), Mexico City, 14000, Mex.  
 SOURCE: Archives of Medical Research (2001), 32(5), 369-393  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Stimulation of central 5-HT1A receptors produces bradycardia and diminishes blood pressure in conscious or anesthetized rats. Our objective was to investigate the effects on blood pressure and heart rate of the partial 5-HT1A receptor agonist and selective .alpha.1D-adrenoceptor antagonist EMY 7378 (8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4.5]decan-7,9-dione hydrochloride) compared to the full 5-HT1A receptor agonist 8-OH-DPAT (8-hydroxy-dipropylamino tetralin) in adult anesthetized rats. Male Wistar rats of 6 mo of age were exposed i.v. (i.v.) to increasing doses of EMY 7378 or 8-OH-DPAT in the absence and presence of WAY 100635. Blood pressure and heart rate were continuously recorded. EMY 7378 induced a decrease in blood pressure with apparent change in heart rate compared to basal values, while 8-OH-DPAT decreased both hemodynamic parameters. EMY 7378 hypotensive effect was antagonized by the selective, silent 5-HT1A receptor antagonist WAY 100635 (N-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-N-(2-pyridinyl)cyclohexanecarboxamide trihydrochloride). However, a remnant yet significant hypotensive effect was not blocked by the antagonist. In contrast, 8-OH-DPAT actions were completely blocked by WAY 100635. Data suggest that EMY 7378 cardiovascular effects are related to activation as a full agonist of central 5-HT1A receptors in adult rats; however, participation of other systems such as vascular .alpha.1-adrenoceptors in

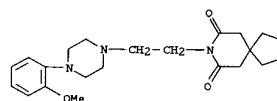
L14 ANSWER 9 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 protein phosphorylation, effect on adenylyl cyclase activity, MAP kinase activation, GTP gamma S binding, and/or inositol phosphate accumulation.  
 Differences in signal transduction due to the .alpha.2 adrenoceptor polymorphisms were obsev. but the polymorphisms have not yet been genetically linked with disease, for example hypertension. The polymorphisms of this invention can be used to det. an individual's risk for developing a disease, for diagnosis, and for selecting appropriate drug treatments based on the identity of the polymorphism.  
 IT 67339-62-2, ANC 239  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polymorphisms in human .alpha.2 adrenergic receptor genes and their diagnostic and therapeutic uses)

RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-

piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 10 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 cardiovascular function is suggested.  
 IT 21102-95-4, EMY 7378  
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)  
 (hypotensive effect of EMY 7378 is antagonized by a silent 5-HT1A receptor antagonist: comparison with 8-OH-DPAT)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

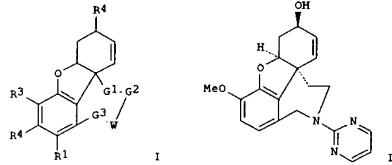


●2 HCl  
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:747793 CAPLUS  
 DOCUMENT NUMBER: 135:304054  
 TITLE: Preparation of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors  
 INVENTOR(S): Jordis, Ulrich; Frehlich, Johannes; Treu, Matthias;  
 Beate; Hirnschall, Manfred; Cziollner, Laszlo; Kaelz, Welzig, Stefan  
 PATENT ASSIGNEE(S): Sanohemica Pharmazeutika Aktiengesellschaft, Austria  
 SOURCE: PCT Int. Appl., 285 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074820	A1	20011011	WO 2001-AT82	20010322
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TO EP 1181294	A1	20020227	EP 2001-914613	20010322
EP 1181294	A1	20020227	EP 2001-914613	20010322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2001005563	A	20020402	BR 2001-5563	20010322
BR 2001005857	A	20020129	NO 2001-5857	20011130
PRIORITY APPLN. INFO.:			AT 2000-546	A 20000331
			AT 2001-238	A 20010215
			WO 2001-AT82	W 20010322
OTHER SOURCE(S):	MARPAT	135:304054		
GI				

L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Galanthamine derivs. and analogs, such as I [R1, R2 = H, Cn, OH, SH, NO2, SO3H, PO3H, NH2, halogen, etc.; R3 = OH, OMe; R4 = OH, alkylxylo, alkenyloxy, alkynyoxy, cycloalkyloxy, arylxy, etc.; G1, G2, G3 = CH2, (CH2)2, (CH2)3, CH(OH), etc.; W = CH2, NR5, etc.], R5 = alkyl, acyl, etc.], were prep'd. for therapeutic use as acetyl- and butyrylcholinesterase inhibitors. Thus, (+-)-galanthamine deriv.

II was prep'd. in 80.8% yield by condensation of (+)-norgalanthamine with 2-chloropyrimidine using NaHCO3 in EtOH. The prep'd. galanthamine derivs.

and analogs were tested for acetyl- and butyrylcholinesterase inhibiting activity. IT 365570-78-9P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of galanthamine analogs for pharmaceutical use as acetyl-

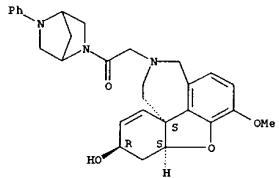
and butyrylcholinesterase inhibitors)

RN 365570-76-9 CAPLUS

CN 2,5-Diaza[2.2.1]heptane, 2-phenyl-5-[[[4aS,6R,8aS]-4a,5,9,10-tetrahydro-6-hydroxy-3-methoxy-6H-benzofuro[3a,3,2-ef][2]benzazepin-11(12H)-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

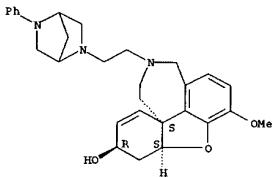
L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 365570-78-1P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors)

RN 365570-78-1 CAPLUS  
 CN 6H-Benzofuro[3a,3,2-ef][2]benzazepin-6-ol,  
 4a,5,9,10,11,12-hexahydro-3-  
 methoxy-11-[2-(5-phenyl-2,5-diazabicyclo[2.2.1]hept-2-yl)ethyl]-,  
 (4aS,6R,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

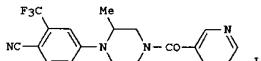
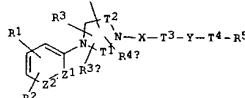


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 12 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:704727 CAPLUS  
 DOCUMENT NUMBER: 135:257268  
 TITLE: Preparation of piperazinylbenzonitrile derivatives and analogs as antiandrogen agents  
 INVENTOR(S): Taniguchi, Nobuaki; Imamura, Masakazu; Kinoyama, Isao; Samizu, Kiyohiro; Kawanami, Eiji; Okada, Minoru; Kotoku, Hiroshi  
 PATENT ASSIGNEE(S): Yamanoichi Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JF 2001261657	A2	20010926	JP 2000-74999	20000317
OTHER SOURCE(S):	MARPAT	135:257268		
GI				



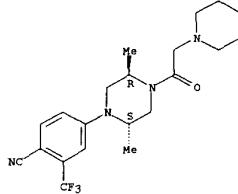
AB The title compds. I [R1, R2 = H, halo, etc.; R3, R3a, R4, R4a = H, alkyl, etc.; T1 = (CH2)m; T2 = (CH2)n; T3 = (Alk1)p; T4 = (Alk2)q; R5 = (un)substituted carbamoyl, etc.; Alk1, Alk2 = (un)substituted alkylene, etc.], m, n = 1 - 3; p, q = 0 or 1; Z1, Z2 = CH, N; Y = bond, O, etc.]

X = CO, etc.], useful as antiandrogen agents (no data), are prep'd. For example, the title compd. II was prep'd.

IT 362471-49-6P RL: BAC (Biological activity or effector, except adverse); BSU (Biological

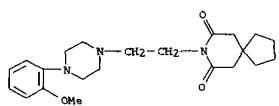
L14 ANSWER 12 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of piperazinylbenzonitrile derivs. and analogs as  
 antiandrogen  
 agents)  
 RN 362471-49-6 CAPLUS  
 CN Piperazine, 1-[4-cyano-3-(trifluoromethyl)phenyl]-2,5-dimethyl-4-(1-  
 piperidinylacetyl), (2S,5R)- (9CI) (CA INDEX NAME)

## Absolute stereochemistry.



L14 ANSWER 13 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:626800 CAPLUS  
 DOCUMENT NUMBER: 135:365674  
 TITLE: Molecular cloning and functional expression of the guinea pig  $\alpha$ .1a-adrenoceptor  
 AUTHOR(S): Gonzalez-Espinosa, C.; Romero-Avila, M. T.;  
 Mora-Ortiz, D. M.; Gonzalez-Espinosa, D.;  
 Garcia-Silva, J.  
 CORPORATE SOURCE: Departamento de Biología Celular, Universidad  
 Nacional Autónoma de México, Instituto de Fisiología  
 Celular, Mexico City, 04510, Mex.  
 SOURCE: European Journal of Pharmacology (2001), 426(3),  
 147-155  
 CODEN: EJPHEZ ISSN: 0014-2999  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal Article  
 LANGUAGE: English  
 AB In the present paper, the cloning and expression of the guinea pig  $\alpha$ .1a-adrenoceptor is presented. The nucleotide sequence had an open reading frame of 1401 bp that encoded a 466 amino-acid protein with an estd. mol. mass of approx.51.5 kDa. When the clone was expressed in COS-1 cells, specific high-affinity binding of [ $^3$ H]prazosin and [ $^3$ H]tamsulosin was obsd. Chloroethylclonidine treatment of membranes slightly decreased the total binding with both radioligands. Binding competition expts. using [ $^3$ H]tamsulosin showed the following potency order: (a) for agonists: norepinephrine > epinephrine > isoproterenol > phenylephrine > norepinephrine > me-thoxamine and (b) for antagonists: prazosin > terazosin > 5-methyl-urapidil > benztropine > phentolamine > mch7. BMY 7378 (8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4.5]decane-7,9-dione). Photoaffinity labeling using [ $^{125}$ I-aryl]azido-prazosin revealed a major broad band with a mol. mass between 70 and 80 kDa. The receptor was functional, as evidenced by an epinephrine-increased prodn. of [ $^{35}$ S]inositol phosphates that was blocked by prazosin.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);  
 PRC (Process)  
 (mol. cloning, functional expression and pharmacol.  
 characterization of  
 guinea pig  $\alpha$ .1a-adrenoceptor)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 13 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

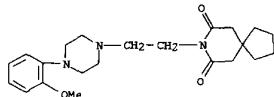


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REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE-  
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L14 ANSWER 14 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:522422 CAPLUS  
DOCUMENT NUMBER: 135:327647  
TITLE: Phe-308 and Phe-312 in transmembrane domains 7 are  
major sites of  $\alpha$ .1-adrenergic receptor  
antagonist binding: imidazoline agonists bind like  
antagonists Waugh, David J. J.; Gaivin, Robert J.; Zuscik,  
AUTHOR(S): Michael J.; Gonzalez-Cabrera, Pedro; Ross, Sean A.; Yun,  
June; Perez, Dianne M.  
CORPORATE SOURCE: Department of Molecular Cardiology NB5, The Lerner  
Research Institute, The Cleveland Clinic  
Foundation, Cleveland, OH, 44195, USA  
SOURCE: Journal of Biological Chemistry (2001), 276(27),  
25366-25371  
PUBLISHER: COSMOS/BCBA3, ISSN: 0021-9258  
DOCUMENT TYPE: American Society for Biochemistry and Molecular  
Biology  
LANGUAGE: English  
AB Although agonist binding in adrenergic receptors is fairly well  
understood and involves residues located in transmembrane domains 3 through 6,  
there are few residues reported that are involved in antagonist binding. In  
fact, a major docking site for antagonists has never been reported in  
any G-protein coupled receptor. It has been speculated that antagonist  
binding is quite diverse depending upon the chem. structure of the  
antagonist, which can be quite different from agonists. We now  
report the identification of two phenylalanine residues in transmembrane domain  
7 of the  $\alpha$ .1a-adrenergic receptor (Phe-312 and Phe-308) that are a  
major site of antagonist affinity. Mutation of either Phe-308 or Phe-312  
resulted in significant losses of affinity (4-1200-fold) for the  
agonists epinephrine,  $\alpha$ -methyl-NMT378, (+)-niguldipine, and  
6-methylurapidil, with no changes in affinity for phenethylamine-type  
agonists such as epinephrine, methoxamine, or phenylephrine.  
Interestingly, both residues are involved in the binding of all  
imidazoline-type agonists such as oxymetazoline, cirazoline, and  
clonidine, confirming previous evidence that this class of ligand  
binds differently than phenethylamine-type agonists and may be more  
antagonist-like, which may explain their partial agonist properties.  
In modeling these interactions with previous mutagenesis studies and  
using the current backbone structure of rhodopsin, we conclude that  
antagonist binding is docked higher in the pocket closer to the extracellular  
surface

L14 ANSWER 14 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
than agonist binding and appears skewed toward transmembrane domain  
7.  
IT 21102-95-4, EMY7378  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES  
(Uses)  
(Phe-308 and Phe-312 in transmembrane domain 7 are major sites of  
alpha1-adrenergic receptor antagonist binding; imidazoline  
agonists  
bind like antagonists)  
RN 21102-95-4 CAPLUS  
CN 8-Azapipro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

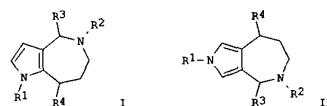


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REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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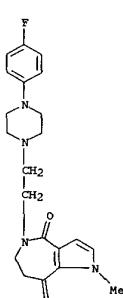
L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:502429 CAPLUS  
DOCUMENT NUMBER: 135:92553  
TITLE: Synthesis and activity of pyrroloazepine derivatives  
INVENTOR(S): Norio Mizuno, Akira Shibata, Makoto Iwamori, Tomo Shimamoto, Tetsuo Nakanishi, Kyoko Inomata,  
Norio PATENT ASSIGNEE(S): Suntory Ltd., Japan  
SOURCE: U.S., 54 pp., Cont.-in-part of U.S. Ser. No.  
875,495.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6258805	B1	20010710	US 1999-312713	19990517
WO 9720845	A1	19970612	WO 1996-JP3522	19961202
W, AU, CA, HU, IL, JP, KR, US			JP 1995-335714	A 19951201
PT, SE	US 5962448	A 19991005	JP 1996-46928	A 19960209
	US 2002072515	A1 20020613	WO 1996-JP3522	W 19961202
PRIORITY APPLN. INFO.:			US 1997-875495	A2 19970621
			US 1999-312713	A1 19990517
OTHER SOURCE(S): MARPAT 135:92553	GI			



AB Synthesis of pyrroloazepine derivs. (I) and (II) [R<sup>1</sup> = H, alkyl, Ph, benzyl; R<sup>2</sup> = substituted alkyl; R<sup>3</sup>, R<sup>4</sup> independently = -O-, -NOH, OH, OMe, SCH<sub>2</sub>CH<sub>2</sub>S] or pharmaceutically acceptable salts for use as 5-HT antagonists is disclosed. Thus, I (R<sup>1</sup> = Me, R<sup>2</sup> = (CH<sub>2</sub>)<sub>2</sub>-piperazinyl-C<sub>6</sub>H<sub>4</sub>F, R<sup>3</sup> = -O-, R<sup>4</sup> = OH) (III) was prepd. by condensation of 3-pyrrolecarboxylic acid with .beta.-alanine Et ester hydrochloride, the amide ester saponified, and the

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
acid cyclized to pyrroloazepine with polyphosphoric acid, the  
azepine N  
alkylated with bromoalkylchloride followed by  
1-(4-fluorophenyl)piperazine  
and reductn. of carbonyl with NaBH<sub>4</sub>. III shows a 90.2% contraction at  
10-7M  
in 5-HT action assay. I and II have strong serotonin-2 receptor  
antagonistic action and low toxicity and less side effects, and are  
therapeutically useful in the treatment of circulatory diseases  
and/or  
conditions related thereto.  
IT 191591-85-2  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation);  
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT  
(Reactant or reagent); USES (Uses)  
(synthesis and activity of pyrroloazepine derivs. as 5-HT  
antagonists)  
RN 191591-85-2 CAPLUS  
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-  
piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



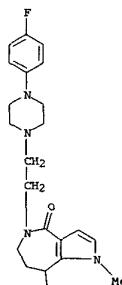
PAGE 1-A

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 2-A

IT 191592-08-2P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic  
use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(synthesis and activity of pyrroloazepine derivs. as 5-HT  
antagonists)  
RN 191592-08-2 CAPLUS  
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-  
piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA  
INDEX NAME)

PAGE 1-A



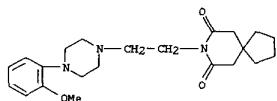
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR  
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PAGE 2-A

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 16 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:473200 CAPLUS  
DOCUMENT NUMBER: 135:283079  
TITLE: Affinity of serotonin receptor antagonists and  
agonists to recombinant and native  
AUTHOR(S): .alpha.1-adrenoceptor subtypes  
Yoshio, Rikar Taniguchi, Takanobu Itoh, Harumi;  
CORPORATE SOURCE: Muramatsu, Ikunobu  
of  
910-1193, Departments of Pharmacology and Radiology, School  
Japan of Medicine, Fukui Medical University, Fukui,  
SOURCE: Japanese Journal of Pharmacology (2001), 86(2),  
189-195  
PUBLISHER: Japanese Pharmacological Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Binding affinities of serotonin (5-HT)-receptor antagonists and  
agonists to human recombinant .alpha.1-adrenoceptor subtypes (.alpha.1a-,  
.alpha.1b- and .alpha.1d-subtypes) were examined and compared with the  
functional affinities obtained in rat caudal artery  
(.alpha.1A-subtype),  
dog carotid artery (.alpha.1B-subtype) and rat thoracic aorta  
(.alpha.1D-subtype). Most of the 5-HT-receptor antagonists and  
agonists tested showed relatively high affinity to the three  
.alpha.1-adrenoceptor subtypes. The highest affinity (close to 1 pM) was found for NAN-190  
(5-HT1A antagonist) in both binding and functional studies.  
5-Methylurapidil (5-HT1A agonist) and EM77378 (5-HT1A agonist) showed  
resp. .alpha.1a(.alpha.1A)- and .alpha.1d(.alpha.1D)-subtype  
selectivity  
in both binding and functional affinities, but spiperone (5-HT2A  
antagonist) showed .alpha.1b-selectivity only in binding affinity.  
The functional affinity of ritanserin (5-HT2A antagonist) to the  
.alpha.1B-subtype was approx. 500-fold lower than that to the  
.alpha.1A-subtype. The results show that many 5-HT-receptor  
antagonists and agonists have high affinity for .alpha.1-adrenoceptors but suggest  
that there is a difference between their functional affinities and  
binding  
affinities in some cases.  
IT 21102-95-4, EMY 7378  
RL: BPR (Biological process); BSU (Biological study, unclassified);  
BIOL (Biological study); PROC (Process)  
(serotonin receptor antagonists and agonists affinity for  
.alpha.1-adrenoceptor subtypes in artery)  
RN 21102-95-4 CAPLUS  
CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

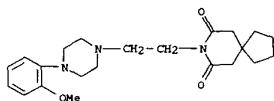
L14 ANSWER 16 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 17 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:434869 CAPLUS  
DOCUMENT NUMBER: 135:29141  
TITLE: Use of .alpha.1 adrenergic receptor  
subtype-selective drugs in patients with acute myocardial infarction  
INVENTOR(S): Schwinn, Debra A.  
PATENT ASSIGNEE(S): Duke University, USA  
SOURCE: PCT Int. Appl., 31 pp.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:  
PATENT NO. KIND DATE APPLICATION NO. DATE  
----- ----- ----- -----  
WO 2001041767 A1 20010614 WO 2000-US33135 20001207  
W: AU, CA, JP  
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,  
NL, PT, SE, TR  
US 200101460 A1 20011018 US 2000-731062 20001207  
PRIORITY APPLN. INFO.: US 1999-169294 P 19991207  
AB The invention discloses the use of .alpha.1a adrenergic  
receptor-selective and/or .alpha.1a/.alpha.1d-selective antagonists in a method of  
preventing restenosis after myocardial infarction and reperfusion. The invention  
further discloses a method of identifying agents suitable for use in  
such a method.  
IT 21102-95-4, EMY-7378  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)  
(.alpha.1 adrenergic receptor subtype-selective drugs in patients  
with acute myocardial infarction, and vascular distribution of .alpha.1  
adrenergic receptor subtypes)  
RN 21102-95-4 CAPLUS  
CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

ACCESSION NUMBER: 2001:321149 CAPLUS

DOCUMENT NUMBER: 135:137465

TITLE: Two Novel and Potent 3-[{o-

Methoxyphenyl)piperazinyl]ethyl]-5-phenylthieno[2,3-d]pyrimidine-2,4-diones Selective for the .alpha.1D Receptor

AUTHOR(S): Carroll, W. A.; Sippy, K. B.; Embenhaze, T. A.; Buckner, S. A.; Hancock, A. A.; Meyer, M. D.

CORPORATE SOURCE: Neurological and Urological Diseases Research, Abbott Laboratories, Abbott Park, IL, 60064-6101, USA

SOURCE: Bioorganic &amp; Medicinal Chemistry Letters (2001), 11(9), 1119-1121

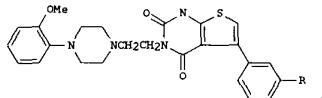
CODEN: BMCLB8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



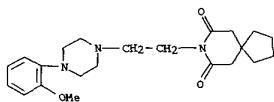
AB The synthesis and in vitro characterization of A-119637 (I, R = H) and A-123189 (I, R = Me), two novel, selective and potent .alpha.1D antagonists, are described.

IT 21102-95-4, EMY7378 255893-38-0, SNAP 8719

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIO (Biological study)

RN 21102-95-4 CAPLUS

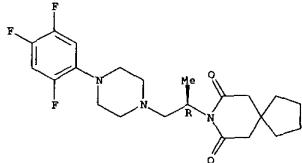
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 255893-38-0 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[{(R)-1-methyl-2-[4-(2,5-trifluorophenyl)-1-piperazinyl]ethyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

ACCESSION NUMBER: 2001:207647 CAPLUS

DOCUMENT NUMBER: 134:305637

TITLE: Failure of AH11110A to functionally discriminate between .alpha.1-adrenoceptor subtypes A, B and D or

AUTHOR(S): Eltze, M.; Konig, H.; Ullrich, B.; Grebe, T.; Byk Gulden, Department of Pharmacology, Konstanz, D-78467, Germany

SOURCE: European Journal of Pharmacology (2001), 415(2,3), 265-276

CODEN: EUPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The potency of the putatively .alpha.1B-adrenoceptor selective drug, 1-[biphenyl-2-yl oxy]-4-imino-4-piperidin-1-yl-butanol (AH11110A), to antagonize contraction upon stimulation of .alpha.1A-adrenoceptors in rat vas deferens and rat perfused kidney, .alpha.1B-adrenoceptors in guinea-pig spleen, mouse spleen and rabbit aorta, and .alpha.1B-adrenoceptors in rat aorta and pulmonary artery was evaluated and compared

to that of a no. of subtype-discriminating antagonists.

N-[3-(4-(2-Methoxyphenyl)-1-piperazinyl)propyl]-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran-8-carboxamide (Rec 15/2739) and

(+,-)-1,3,5-trimethyl-6-[[3-[4-((2,3-dihydro-2-hydroxymethyl)-1,4-benzodioxin-5-yl)-1-piperazinyl]propyl]amino]-2,4(1H,3H)-pyrimidinedione (BB805-033) were confirmed as selective for .alpha.1A-adrenoceptors, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4.5]decane-7,9-dione (EMY

7379),

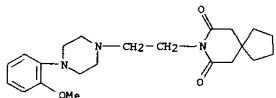
8-[2-(1,4-benzodioxan-2-ylmethylamino)ethyl]-8-azaspiro[4.5]decane-7,9-dione (MDL 73005EP), and cysteazocin were found to be selective for .alpha.1B-adrenoceptors, whereas spiperone was weakly selective for .alpha.1B-over .alpha.1A-adrenoceptors. However, from the functional affinity profile obtained for AH11110A at .alpha.1A-adrenoceptors (pA<sub>2</sub>=6.41 in rat vas deferens), .alpha.1B-adrenoceptors

(pA<sub>2</sub>=5.40-6.54) and .alpha.1B-adrenoceptors (pA<sub>2</sub>=5.47-5.48) the affinity and presumed selectivity previously obtained for AH11110A in radioligand binding studies at most .alpha.1B-and claimed .alpha.1B-adrenoceptors (pKi=7.10-7.73) could not be confirmed. Addnl., AH11110A enhanced the general contractility of rat vas deferens, produced a bell-shaped dose-response curve of vasodilation in perfused rat kidney, and its antagonism in most other tissues was not simply competitive. The

affinity of AH11110A for prejunctional .alpha.2-adrenoceptors in rabbit vas deferens (pA<sub>2</sub>=5.44) was not much lower than that displayed for .alpha.1-adrenoceptor subtypes, revealing that AH11110A, besides .alpha.1-adrenoceptors, also interacts with .alpha.2-adrenoceptors,

and thus may be unsuitable for .alpha.-adrenoceptor subtype characterization.

L14 ANSWER 19 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 at least in smooth muscle contg. functional studies.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BPR  
 (Biological process); BSU (Biological study, unclassified); BIOL (Biological  
 study);  
 PROC (Process)  
 (failure of AH11110A to functionally discriminate between  
 .alpha.1-adrenoceptor subtypes A, B and D or between .alpha.1- and  
 .alpha.2-adrenoceptors in animal tissues as compared with other  
 agents)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



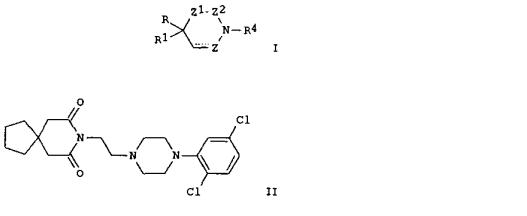
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REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 2001:63974 CAPLUS  
 DOCUMENT NUMBER: 134:115867  
 TITLE: Preparation of azapirodecano(diones and analogs  
 as  
 INVENTOR(S): Gianni, Testa, Rodolfo  
 PATENT ASSIGNEE(S): Recordati Industria Chimica e Farmaceutica S.p.A., Italy; Recordati S.A., Chemical and Pharmaceutical Company  
 SOURCE: PCT Int. Appl. 67 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005765	A1	20010125	WO 2000-EP6738	20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, N, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG IT 99MI1578 A1 20010115 IT 1999-MI1578 19990715 EP 1200406 A1 20020502 EP 2000-945917 20000714 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL PRIORITY APPLN. INFO.: IT 1999-MI1578 A 19990715 WO 2000-EP6738 W 20000714 OTHER SOURCE(S): MARPAT 134:115867 GI				

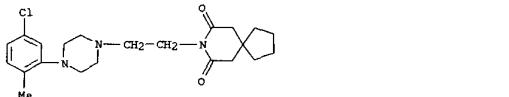
L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



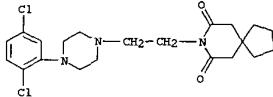
AB Title compds. [I; R, R1 = H or alkyl; RR1 = (CH2)2-6; R4 = CH3CHR7CHR3; R3 = H or alkyl; R7 = Z324R2; R2 = halo, alkyl, cyano; Z = CH2, CO, CH, 21 - bond or CH2; 22 = CH2 or CO; Z3 = piperidine- or -azine-1,4-diyl or NMe(CH2)mZ24R2; Z4 = (un)substituted 1,2-phenylene; Z5 = O, S, NH, NMe; m = 2-4; dashed line = optional addnl. bond] were prep'd. Thus, 8-(2-bromoethyl)-8-azapiro[4.5]decano-7,9-dione was aminated by 1-(2,5-dichlorophenyl)piperazine to give title compd. II. Data for biol.

activity of I were given.  
 IT 255893-42-6P 321601-67-6P 321601-68-7P  
 321601-70-1P 321601-71-2P  
 321601-72-3P 321601-73-4P  
 321601-75-6P 321601-76-7P 321601-77-8P  
 321601-78-9P 321601-79-0P 321601-80-3P  
 321601-81-4P 321601-82-5P 321601-83-6P  
 321601-84-7P 321601-87-0P 321601-89-2P  
 321601-90-5P 321601-91-6P 321601-92-7P  
 321601-93-8P 321601-94-9P 321601-95-0P  
 321601-96-1P 321601-97-2P 321602-28-2P  
 321602-36-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prep'n. of azapirodecano(diones and analogs as .alpha.1D  
 adrenoceptor  
 antagonists)  
 RN 255893-42-6 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(5-chloro-2-methylphenyl)-1-  
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

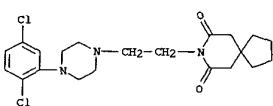


RN 321601-67-6 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 321601-68-7 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1  
 CRN 321601-67-6  
 CMF C21 H27 Cl2 N3 O2



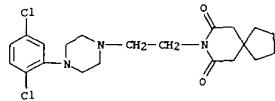
CM 2  
 CRN 75-75-2  
 CMF C H4 O3 S



RN 321601-69-8 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, dimethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 321601-67-6  
CMF C21 H27 Cl2 N3 O2

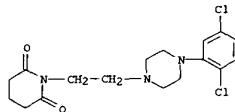


CM 2

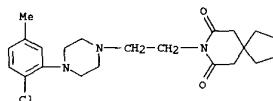
CRN 75-75-2  
CMF C H4 O3 S



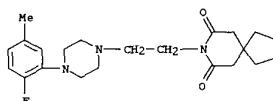
RN 321601-70-1 CAPLUS  
CN 2,6-Piperidinediones,  
1-(2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl)- (9CI) (CA INDEX NAME)



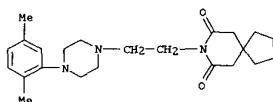
RN 321601-71-2 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



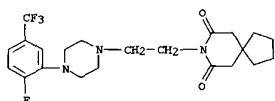
RN 321601-72-3 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-fluoro-5-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



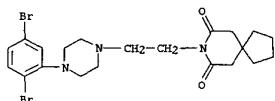
RN 321601-73-4 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



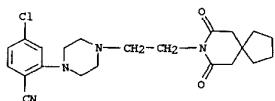
RN 321601-74-5 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-[2-fluoro-5-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



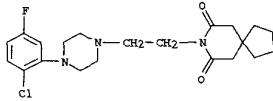
RN 321601-75-6 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dibromophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



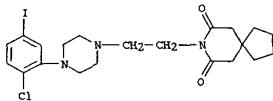
RN 321601-76-7 CAPLUS  
CN Benzonitrile,  
4-chloro-2-[4-(7,9-dioxo-8-azaspiro[4.5]dec-8-yl)ethyl]- (9CI) (CA INDEX NAME)



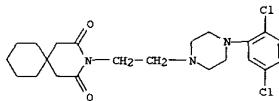
RN 321601-77-8 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



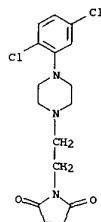
RN 321601-78-9 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-iodophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



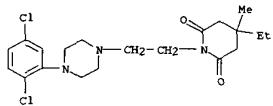
RN 321601-79-0 CAPLUS  
CN 3-Azaspiro[5.5]undecane-2,4-dione, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



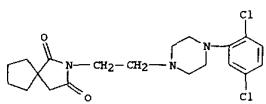
RN 321601-80-3 CAPLUS  
CN 2,5-Pyrrolidinedione,  
1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



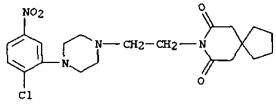
RN 321601-81-4 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-4-  
ethyl-4-methyl- (9CI) (CA INDEX NAME)



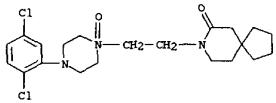
RN 321601-82-5 CAPLUS  
CN 2-Azaspiro[4.4]nonane-1,3-dione, 2-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



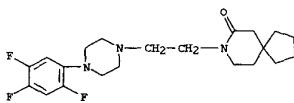
RN 321601-83-6 CAPLUS  
CN 7-Azaspiro[3.5]nonane-6,8-dione, 7-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



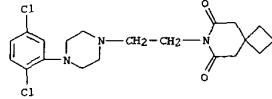
RN 321601-91-6 CAPLUS  
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



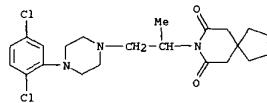
RN 321601-92-7 CAPLUS  
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,4,5-trifluorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



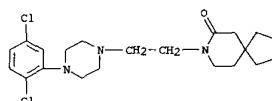
RN 321601-93-8 CAPLUS  
CN 3-Azaspiro[5.5]undecan-2-one, 3-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



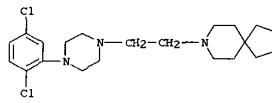
RN 321601-84-7 CAPLUS  
CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



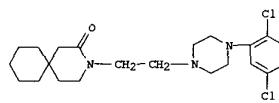
RN 321601-87-0 CAPLUS  
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



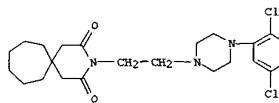
RN 321601-89-2 CAPLUS  
CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



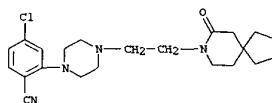
RN 321601-90-5 CAPLUS



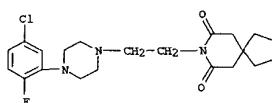
RN 321601-94-9 CAPLUS  
CN 3-Azaspiro[5.6]dodecane-2,4-dione, 3-[2-[4-(2,5-dichlorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



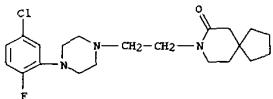
RN 321601-95-0 CAPLUS  
CN Benzonitrile,  
4-chloro-2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl- (9CI) (CA INDEX NAME)



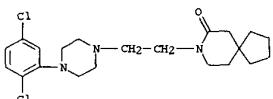
RN 321601-96-1 CAPLUS  
CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(5-chloro-2-fluorophenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RN 321601-97-2 CAPLUS  
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-(4-(5-chloro-2-fluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

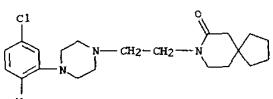


RN 321602-28-2 CAPLUS  
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-(4-(2,5-dichlorophenyl)-1-piperazinyl)ethyl], monohydrochloride (9CI) (CA INDEX NAME)



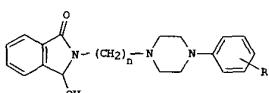
● HCl

RN 321602-36-2 CAPLUS  
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-(4-(5-chloro-2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



IT 321602-22-6P 321602-24-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(prepn. of azaspipredane(diones and analogs as .alpha.1D adrenoceptor antagonists)

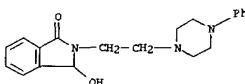
L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000-780228 CAPLUS  
DOCUMENT NUMBER: 134:71569  
TITLE: Preparation of N-[.omega.- (4-aryl-1-piperazinyl)ethyl]propyl-3-hydroxypthalimidines  
AUTHOR(S): Desai, R. A.; Samant, S. D.  
CORPORATE SOURCE: Organic Chemistry Research Laboratory, University Department of Chemical Technology, Mumbai, 400 019,  
INDIA  
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (2000), 39(16), 455-457  
CODEN: IJSBBD; ISSN: 0376-4699  
PUBLISHER: National Institute of Science Communication, CSIR  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 134:71569  
GI



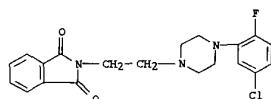
I

AB The reaction of .omega.- (4-aryl-1-piperazinyl)ethyl/propyl amine with 3-hydroxypthalimidone furnishes the title compds. I (n = 2, 3; R = H, 2-, 3-, 4-Me, Cl) along with minor amt. of the corresponding N-[.omega.- (4-aryl-1-piperazinyl)ethyl]propyl-2-formylbenzamides.  
IT 316146-14-2P 316146-15-3P 316146-17-5P  
316146-20-0P 316146-22-2P 316146-24-4P  
316146-26-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

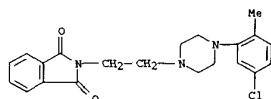
RN 316146-14-2 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RN 321602-22-6 CAPLUS  
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

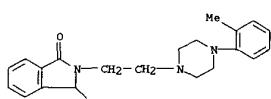


RN 321602-24-8 CAPLUS  
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

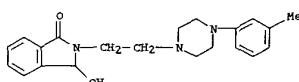


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

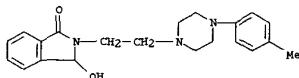
L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RN 316146-15-3 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



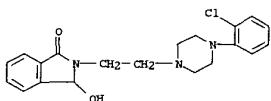
RN 316146-17-5 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-(3-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



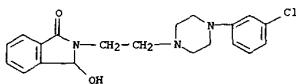
RN 316146-20-0 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-(4-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



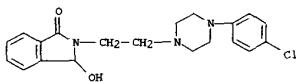
RN 316146-22-2 CAPLUS  
CN 1H-Isoindol-1-one, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RN 316146-24-4 CAPLUS  
CN 1H-Isoindol-1-one, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



RN 316146-26-6 CAPLUS  
CN 1H-Isoindol-1-one, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)

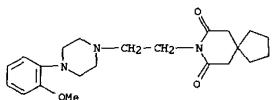


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 22 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:779744 CAPLUS  
DOCUMENT NUMBER: 134:857  
TITLE: An .alpha.1A/.alpha.1B-adrenoceptor mediates contraction of canine subcutaneous resistance arteries

AUTHOR(S): Argyle, Sally Anne; McGrath, John Christie  
CORPORATE SOURCE: Neuroscience  
Life Sciences, University of Glasgow, Glasgow, UK  
SOURCE: Journal of Pharmacology and Experimental Therapeutics  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB To determine the characteristics of the .alpha.1-adrenoceptor subtypes involved in adrenergic regulation of peripheral vascular resistance, contraction of canine s.c. resistance arteries was studied using wire myographs. The potencies of agonists and antagonists, chosen for their ability to discriminate between .alpha.1-adrenoceptor subtypes, were assessed in the presence of cocaine (3 μM), corticosterone (30 μM), and propranolol (1 μM). The rank order of agonist potency ( $pEC_{50}$ ) was (R)-A-61603 (7.88±0.01) > norepinephrine (6.41±0.01) > phenylephrine (5.93±0.01). The high sensitivity to (R)-A-61603 relative to phenylephrine is inconsistent with the presence of the .alpha.1B-adrenoceptor and most consistent with an .alpha.1A-adrenoceptor response. This is supported by the low affinity for the .alpha.1B-selective antagonist BMY 7378 ( $pK_B$  6.51±0.47). The low  $pA_2$  values for prazosin (8.36) and HVT23 (8.81), by definition, indicate the involvement of the putative .alpha.1B-adrenoceptor, a hypothesis supported by the  $pA_2$  values for WB4101 (8.42) and 5-methyl-urapidil (8.08). Pre-exposure to 1 μM CGC had little effect, whereas 100 μM CGC reduced the max. contraction but not the sensitivity to norepinephrine. This low sensitivity to CGC argues against the presence of the .alpha.1B-adrenoceptor. We conclude that, by current definitions, an .alpha.1A/.alpha.1B-adrenoceptor causes contraction of these vessels. This does not support the concept that selectivity for the .alpha.1A-adrenoceptor is the basis for the effectiveness of some .alpha.-blockers in some tissues, such as prostate, but not in other tissues such as blood vessels. Rather, the generally low potency of .alpha.-blockers in some tissues may be due to a tissue-specific property.

L14 ANSWER 22 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
of the receptors.  
IT 21102-95-4 BMY 7378  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(.alpha.1A/.alpha.1B-adrenoceptor mediates contraction of canine s.c. resistance arteries)  
RN 21102-95-4 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (SCI) (CA INDEX NAME)

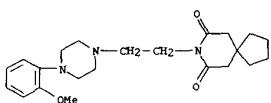


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REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 23 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:575753 CAPLUS  
DOCUMENT NUMBER: 134:51220  
TITLE: Pharmacological characterization of [<sup>3</sup>H]-JTH-601, a novel .alpha.1-adrenoceptor antagonist binding to recombinant human .alpha.1-adrenoceptors and human prostates

AUTHOR(S): Takahashi, Masahiko; Taniguchi, Takanobu  
Kanamaru, Hiroshi; Okada, Kenichiro; Muramatsu, Ikuonobu  
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan  
SOURCE: Life Sciences (2000), 67(20), 2443-2451  
CODEN: LIFSAK; ISSN: 0024-3205  
PUBLISHER: Elsevier Science Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Several .alpha.1-adrenoceptor (AR) selective antagonists are now widely used to improve lower urinary tract symptoms in benign prostatic hyperplasia patients. However, these drugs often result in orthostatic hypotension, because of their poor uroselectivity: the blockade of .alpha.1B-AR not only in prostate but also in vasculature. Here we have investigated uroselectivity of JTH-601, a newly developed antagonist, in radioligand binding expt. using recombinant human .alpha.1-AR subtypes and human prostate. In satn. expts., [<sup>3</sup>H]-JTH-601 showed subtype selectivity with high affinity to .alpha.1A-AR ( $pK_D$ : 9.88±0.09), lower affinity to .alpha.1B-AR ( $pK_D$ : 8.96±0.17) and no specific binding at concns. up to 3000 pm to .alpha.1D-AR. In competition expts., JTH-601 and its metabolic compd. (JTH-601-G1) also showed .alpha.1A-AR selectivity, exhibiting approx. 5 times higher affinity for .alpha.1A-AR than for .alpha.1B-AR, 10 to 20 times higher affinity than for .alpha.1D-AR, resp. [<sup>3</sup>H]-JTH-601 also bound to human prostate membranes in stoichiometric manner with high affinity const. ( $pK_D$ : 9.89±0.12,  $B_{max}$ =123.6,±16 fmol/mg protein). JTH-601 is a unique .alpha.1-AR antagonist that shows high affinity and selectivity for human recombinant .alpha.1A- and human prostate. This new compd. is useful for understanding .alpha.1-AR pharmacol. and may have a therapeutic value.  
IT 21102-95-4, BMY7378  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L14 ANSWER 23 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (phenoxyl) characterization of (3H)-JTM-601, a novel  
 .alpha.1-adrenoceptor antagonist binding to recombinant human  
 .alpha.1-adrenoceptors and human prostates)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

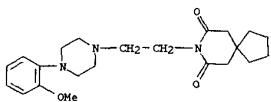


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 REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L14 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 (Continued)  
 (phenoxy) characterization of (3H)-JTM-601, a novel  
 .alpha.1-adrenoceptor antagonist binding to recombinant human  
 .alpha.1-adrenoceptors and human prostates)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

114 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:719190 CAPLUS  
 DOCUMENT NUMBER: 133:344153  
 TITLE: Development of scintillation-proximity assays for  
 alpha adrenoceptors  
 AUTHOR(S): Gobel, J.; Saussey, D. L.; Goetz, A. S.  
 CORPORATE SOURCE: Wellcome  
 Research and Development, Research Triangle Park,  
 NC,  
 SOURCE: 27709, USA  
 Methods Journal of Pharmacological and Toxicological  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Binding assays have long been used to det. compd. affinity and  
 selectivity for various seven-transmembrane receptors. Over time, the degree of  
 complexity has significantly reduced, whereas the throughput of the  
 various assays has greatly increased. In this article, the authors  
 detail the development of a filter-binding assay and a  
 scintillation-proximity  
 assay (SPA) designed to quantify a compd.'s affinity for the three  
 .alpha.1-adrenoceptor subtypes, .alpha.1A, .alpha.1B, and .alpha.1D.  
 The various components of the assays such as ease of assay performance,  
 robustness, cost, and generation of radioactive waste are compared and  
 contrasted. On the basis of the results, the SPA offers many  
 advantages of high-throughput assay formats over the traditional filter-binding  
 assay. To follow up on the success of the .alpha.1-adrenoceptor SPA,  
 SPAs for the three .alpha.2-adrenoceptors were developed and are detailed  
 in this article. Affinity data generated for a select no. of .alpha.2  
 compds. agree with reported literature values. These assays, like  
 those for .alpha.1 subtypes, are very amenable to high-throughput screening  
 campaigns. In conclusion, scintillation-proximity assays offer  
 significant advantages over filter-binding assays.  
 IT 21102-95-4, BM7378  
 RL: ANI (Analytical); BPR (Biological process); BSU (Biological study,  
 unclassified); ANSI (Analytical study); BIOL (Biological study); PROC  
 (Process); (scintillation-proximity assays to quantify compd.'s affinity for  
 alpha adrenoceptor subtypes)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

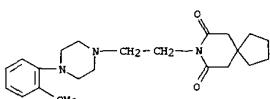
L14 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L14 ANSWER 25 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:667305 CAPLUS  
 DOCUMENT NUMBER: 133:359442  
 TITLE: .alpha.1-Adrenoceptors in the guinea pig thoracic  
 aorta  
 AUTHOR(S): Yamamoto, Yoshiharu; Koike, Katsuo  
 CORPORATE SOURCE: Department of Chemical Pharmacology, Toho  
 University  
 School of Pharmaceutical Sciences, Chiba,  
 274-8510,  
 SOURCE: Japan  
 Journal of Smooth Muscle Research (1999), 35(5,6),  
 181-192  
 PUBLISHER: Japanese Society of Smooth Muscle Research  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In the present study, the authors tried to det. which .alpha.1-  
 adrenoceptor subtypes are involved in the guinea pig thoracic aorta by  
 using in vitro functional anal. Firstly, the authors tried to est.  
 the pA2 values of some key .alpha.1-adrenoceptor antagonists (prazosin,  
 5-methylurapidil, WB4101, BM7378 and tamulosin) against responses to  
 norepinephrine in the thoracic aorta of guinea pigs. The  
 concn.-response  
 curves of norepinephrine were rightward shifted by the presence of  
 prazosin, 5-methylurapidil, WB4101, BM7378 and tamulosin. The pA2  
 values for these antagonists against norepinephrine were 7.63, 7.78,  
 8.20,  
 5.73 and 9.57, resp. Secondly, the authors tried to compare the  
 estd. pA2  
 values obtained in the present study with reported pKi and pA2 values  
 for  
 cloned and native .alpha.1-adrenoceptor subtypes. In rabbit  
 mesenteric  
 artery, trigone, urethra, prostate and human lower urinary tract which  
 were proposed to contain the putative .alpha.1L-adrenoceptor, the  
 authors  
 obtained a good correlation for the pA2 values reported in these  
 tissues  
 with pA2 values estd. in guinea pig thoracic aorta. Moreover,  
 regression  
 lines were close to the line of identity. These results suggest that  
 the .alpha.1-adrenoceptors mediating contraction of guinea pig thoracic  
 aorta  
 are similar pharmacol. to the putative .alpha.1L-adrenoceptor subtype  
 in  
 rabbit mesenteric artery, trigone, urethra, prostate and human lower  
 urinary tract. As a final point, guinea pig thoracic aorta may be  
 used as  
 a tool to develop new .alpha.1-adrenoceptor antagonists  
 therapeutically  
 advantageous in the treatment of urinary tract obstruction (e.g., in  
 benign prostatic hyperplasia).  
 IT 21102-95-4, BM7378  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological)

L14 ANSWER 25 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 study, unclassified); BIOL (Biological study)  
 (alpha-1-adrenoceptor antagonist; alpha-1-adrenoceptor subtypes  
 mediating vasoconstriction in guinea pig thoracic aorta)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4,5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



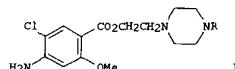
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REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 26 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 study, unclassified); BIOL (Biological study)  
 (alpha-1-adrenoceptor antagonist; alpha-1-adrenoceptor subtypes  
 mediating vasoconstriction in guinea pig thoracic aorta)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4,5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

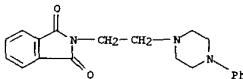
AUTHOR(S): Ivan  
 CORPORATE SOURCE: Innovation  
 SOURCE: Paris-Sud, Chatenay-Malabry, 92296, Fr.  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 133:362752  
 GI

Giner, Mireille; Berque-Bestel, Isabelle; Miallet, Jeanne; Lezoualc'h, Frank; Donzeau-Gouge, Patrick; Sicic, Sames; Fischmeister, Rodolphe; Langlois, Michel  
 INSERM U-446 Institut de Signalisation et de Therapeutique (IFR-151) Faculte de Pharmacie, CNRS-BIOCIS (UPRES A 8076) and Laboratoire de Cardiologie Cellulaire et Moleculaire Universite de Paris-Sud, Chatenay-Malabry, 92296, Fr.  
 Journal of Medicinal Chemistry (2000), 43(20), 3761-3769  
 CODEN: JMCHAR; ISSN: 0022-2623  
 American Chemical Society  
 Journal  
 English  
 CASREACT 133:362752



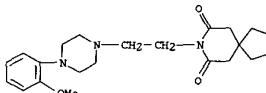
AB New derivs. of arylpiperazine I [R = (un)substituted Ph, 1-naphthyl, CO2Et, CO2CHMe3, Me, H, pyrimidinyl, pyrazinyl, pyridazinyl, pyridinyl]  
 were designed from ML 10302, a potent 5-HT4 receptor agonist in the gastrointestinal system. They were synthesized by condensation of the arylpiperazines or heteroarylpirperazines with 2-bromoethyl 4-amino-5-chloro-2-methoxybenzoate. They were evaluated in binding assays on the recently cloned human 5-HT4(e) isoform stably expressed in C6 glial cells with [<sup>3</sup>H]GR 113808 as the radioligand. The affinity values (K<sub>i</sub>) depended upon the substituent on the arom. ring. A chlorine atom produced a marked drop in activity (K<sub>i</sub> > 100 nM), while a m-methoxy group gave a compd. with nanomolar affinity (K<sub>i</sub> = 3 nM). The most potent compds. were the heterocyclic derivs. with pyrimidine, pyrazine, pyridazine, or pyridine moieties. K<sub>i</sub> values for I [R = Ph, 2-pyrimidinyl] were detd. for

L14 ANSWER 26 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 the 5-HT4(a), 5-HT4(b), 5-HT4(c), and 5-HT4(d) receptor isoforms transiently expressed in COS cells. The results indicated that the compds. were not selective. They produced an inhibition of the 5-HT-stimulated cAMP synthesis in the C6 glial cells stably expressing the 5-HT4(e) receptor and shifted the 5-HT concn.-effect curve on adenylyl cyclase activity with pED<sub>5</sub> values of 7.44 and 8.47, resp. In isolated human atrial myocytes, I [R = 2-pyrimidinyl] antagonized the stimulatory effect of 5-HT on the L-type calcium current (I<sub>Ca</sub>) with a KD value of 0.7 nM.  
 IT 75000-24-7  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (arylpirperazinylethyl aminobenzoates as antagonists of the human cloned 5-HT4 receptor isoforms)  
 RN 75000-24-7 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 27 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 study, unclassified); BIOL (Biological study)  
 (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 Effects of the 5HT1A agonist/antagonist BMY 7378 on light-induced phase advances in hamster circadian activity rhythms during aging  
 AUTHOR(S): Byku, Mirnela; Gannon, Robert L.  
 CORPORATE SOURCE: Department of Biology, Dowling College, Oakdale, NY, 11769, USA  
 SOURCE: Journal of Biological Rhythms (2000), 15(4), 300-305  
 PUBLISHER: Sage Science Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB BMY 7378 was a highly effective chronobiotic that more than doubled the magnitude of light-induced phase shifts in hamster wheel-running activity rhythms. Light-induced phase advances of >10eq.6 h in hamster wheel-running activity following a single systemic dose of BMY 7378 were obsd. Furthermore, the BMY 7378 potentiation of phase shifts was maintained in old hamsters, suggesting that BMY 7378 has a different site of activity than that of previously reported 5HT1A agonists that have a diminished effect on circadian phase during aging.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (serotonergic/5HT1A agonist/antagonist BMY 7378 effect on light-induced phase advances in circadian activity during aging)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4,5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



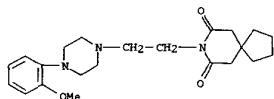
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REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 27 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
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FORMAT

L14 ANSWER 28 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:558944 CAPLUS  
DOCUMENT NUMBER: 133:276210  
TITLE: Tissue selectivity of XMD-3213, an  
prostate .alpha.1-adrenoceptor antagonist, in human  
and vasculature  
AUTHOR(S): Murata, Satoshi; Taniguchi, Takanobu; Takahashi,  
Masahiko; Okada, Kenichiro; Akiyama, Katuyoshi;  
Muramatsu, Ikuonobu  
CORPORATE SOURCE: Department of Pharmacology and Urology, School of  
Medicine, Fukui Medical University, Matsuoka,  
Japan  
SOURCE: Journal of Urology (Baltimore) (2000), 164(2),  
578-583  
CODEN: JOURAA ISSN: 0022-5347  
PUBLISHER: Lippincott Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB We evaluated the binding and functional affinity of XMD-3213 and other  
.alpha.1-adrenoceptor (AR) antagonists such as prazosin or  
tamsulosin, to  
compare the tissue selectivity of these antagonists between human  
prostate and vasculature. In the binding expts., satn. expts. using [<sup>3</sup>H]-XMD  
and [<sup>3</sup>H]-prazosin (PZ) were performed, and competition of [<sup>3</sup>H]-PZ binding  
by

L14 ANSWER 28 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
prostate and by .alpha.1B-AR in the mesenteric artery. These results  
suggest that XMD-3213 is a substantially prostate-selective  
.alpha.1-adrenoceptor antagonist in human tissues compared with other .alpha.1-AR  
antagonists.  
IT 21102-95-4, BMY7378  
RL: BAC (Biological activity or effector, except adverse); BPR  
(Biological  
process); BSU (Biological study, unclassified); BIOL (Biological  
study);  
PROC (Process)  
(tissue selectivity of XMD-3213 and other .alpha.1-adrenoceptor  
antagonists in human prostate and vasculature)  
RN 21102-95-4 CAPLUS  
CN 8-Acetoxy[4.5]deca-7,9-diene, 8-[2-(4-(2-methoxyphenyl)-1-  
piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

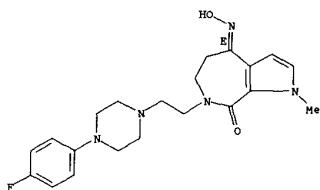


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REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE  
FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 29 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:554947 CAPLUS  
DOCUMENT NUMBER: 133:281710  
TITLE: Studies on antihypertensive agents with  
antithrombotic  
activity. 2. Syntheses and pharmacological  
evaluation  
of pyrrolo[2,3-c]azepine derivatives  
AUTHOR(S): Mizuno, Akira; Miya, Mikiko; Kamei, Tomoe;  
Shibata,  
Takiguchi,  
Makoto; Tatsuka, Toshio; Nakanishi, Kyoko;  
Inomata,  
Chikako; Hidaka, Toshinori; Yamaki, Akira;  
Norio  
CORPORATE SOURCE: Suntory Institute for Biomedical Research, Osaka,  
618-8503, Japan  
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(8),  
1129-1137  
CODEN: CPBTAL ISSN: 0009-2363  
PUBLISHER: Pharmaceutical Society of Japan  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A series of 7-aminoalkylpyrrolo[2,3-c]azepine derivs. was synthesized  
and  
evaluated as .alpha.1-adrenergic and 5-HT2 receptor antagonists, with  
the  
aim of finding a novel potent antihypertensive agent with both  
activities.  
Among the compds. obtained in this study, (E)-1-ethyl-7-[3-[4-(4-  
fluorophenyl)piperazin-1-yl]propyl]-4-hydroxymimo-1,4,5,6,7,8-  
hexahydropyrrolo[2,3-c]azepin-8-one (I) displayed potent  
.alpha.1-adrenoceptor blocking activity ( $pA_2 = 7.83 \pm 0.20$ ) and  
5-HT2-receptor blocking activity ( $pA_2 = 9.47 \pm 0.17$ ) in isolated  
guinea  
pig arteries. At 3 mg/kg oral administration, I exhibited  
antihypertensive activity more potent than that of doxazosin in  
desoxycorticosterone acetate (DOCA)-salt hypertensive dogs.  
Furthermore,  
this compd. reduced the rate of mouse acute pulmonary thromboembolic  
death induced by collagen and serotonin at oral doses of 0.3 mg/kg or  
more, and its effect lasted for at least 6 h at 3 mg/kg.  
IT 300548-34-9  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
study); PREP (Preparation)  
(prep. of aminealkylpyrroloazepinediones with .alpha.-adrenergic  
and  
5-HT2 antagonist activity)  
RN 300548-34-9 CAPLUS  
CN Pyrrolo[2,3-c]azepine-4,8(1H,5H)-dione, 7-[2-(4-(4-fluorophenyl)-1-  
piperazinyl)ethyl]-6,7-dihydro-1-methyl-, 4-oxime, (4E)- (9CI) (CA  
INDEX  
NAME)

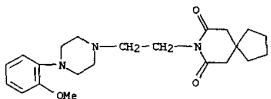
Double bond geometry as shown.



REFERENCE COUNT:  
FOR THIS  
FORMAT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE  
RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 30 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:536311 CAPLUS  
DOCUMENT NUMBER: 134:157834  
TITLE: Quantitative imaging in live human cells reveals intracellular .alpha.1-adrenoceptor ligand-binding sites  
AUTHOR(S): Mackenzie, Janet F.; Daly, Craig J.; Padiani,  
John D., McGrath, John C.  
CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience & Biomedical Sciences, Institute of Biomedical & Life Sciences, University of Glasgow, Glasgow, UK  
SOURCE: Journal of Pharmacology and Experimental Therapeutics  
(2000), 294(2), 434-443  
CODEN: JPETAB; ISSN: 0022-3565  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Cellular distribution and binding characteristics of native .alpha.1-adrenoceptors (ARs) were detd. in a live, single, human smooth muscle cell (SMC) with confocal laser scanning microscopy and a fluorescent ligand, BODIPY-FL prazosin (QAPB). This allowed single-cell competitive ligand binding and showed that 40% of .alpha.1-AR-binding sites in native cells are intracellular. QAPB had high affinity and acted as a nonselective, competitive antagonist vs. [<sup>3</sup>H]prazosin at cloned human .alpha.1a-, .alpha.1b-, and .alpha.1d-AR subtypes on membrane preps. and whole cells. RS100329 had 70-fold selectivity for .alpha.1a-ARs vs. .alpha.1b- and .alpha.1d-ARs, validating its use to identify this subtype. In similar cells QAPB-assocd. fluorescence provided quant. data analogous and comparable to [<sup>3</sup>H]prazosin binding in whole cells. In human, dissocd., prostatic smooth muscle cells QAPB-assocd. fluorescence binding exhibited specific high-affinity binding properties (FKD = 0.63 ± 0.02 nM), which was 3- to 4-fold higher compared with recombinant cells (FKD = 2.1-2.3 nM). Internal consistency in the data showed that affinity is greater, in general, in membrane preps. than in cells but also greater in the native prostatic tissues or cells than in equiv. recombinant receptors. Fluorescence revealed binding sites both on the plasmalemmal membrane and on intracellular compartments: at all locations RS100329 inhibited QAPB binding identifying the sites as .alpha.1a-ARs. Quant. three-dimensional mapping of QAPB-assocd. fluorescence binding in native

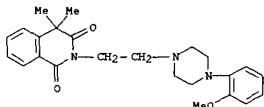
L14 ANSWER 30 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
human cells showed that 40% of high-affinity-binding sites was in intracellular compartments. This provides a potential new site for physiol. agonism and makes intracellular access a potential differentiator of drug action.  
IT 21102-95-4, BM77378  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
.alpha.1-adrenoceptor ligand-binding sites are intracellularly localized in live human prostatic smooth muscle cells)  
RN 21102-95-4 CAPLUS  
CN 6-Azaspiron(4,5)decano-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



• HCl  
REFERENCE COUNT:  
FOR THIS  
FORMAT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE  
RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 31 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:458289 CAPLUS  
DOCUMENT NUMBER: 133:130140  
TITLE: Characterization of the .alpha.2-adrenoceptor subtype,  
which functions as .alpha.2-autoreceptor in human neocortex  
AUTHOR(S): Feuerstein, Thomas J.; Huber, Boris; Vetter, Jan; Aranda, Heike; Van Velthoven, Vera; Limberger, Norbert  
CORPORATE SOURCE: Sektion Klinische Neuropharmakologie der Neurologischen Universitätsklinik, Freiburg,  
D-79106,  
SOURCE: Germany  
Therapeutics  
(2000), 294(1), 356-362  
CODEN: JPETAB; ISSN: 0022-3565  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The pharmacol. properties of the .alpha.2-adrenergic receptors regulating the release of norepinephrine were investigated in human neocortex. Slices were preincubated with [<sup>3</sup>H]norepinephrine, superfused under blockade of transmitter reuptake, and stimulated elec. First, the autoinhibitory circuit of [<sup>3</sup>H]norepinephrine release was analyzed quant. by estn. of the K<sub>d</sub> of norepinephrine at the .alpha.2-autoreceptor (10-7.99 M), the concn. of the endogenous transmitter causing this autoinhibition at a stimulation frequency of 3 Hz (10-7.61 M), and the max. inhibition obtainable through the autoreceptor (93%). Second, antagonist pK<sub>b</sub> values of nine antagonists were detd. by using their pEC<sub>50</sub> values (neg. logarithms of antagonist concns. that increased the elec. evoked overflow of tritium by 50%) against the release-inhibiting effect of the endogenous transmitter. When compared with binding or functional data from the literature, the pK<sub>b</sub> values correlated best with the antagonist affinities at .alpha.2A binding sites. In contrast, the correlations with .alpha.2B, .alpha.2C, and .alpha.2D sites were not as good. It is concluded that in human neocortex prejunctional autoreceptors are .alpha.2A.  
IT 67339-62-2, AR239  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(norepinephrine release from human neocortex and calcn. of unbiased

L14 ANSWER 31 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 dissoch. consts. of antagonists in relation to characterization of  
 .alpha.1-adrenoceptor subtype which functions as  
 .alpha.2-autoreceptor  
 (in human neocortex)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isquinolinidine, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



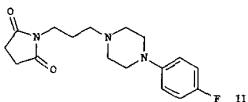
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000-455285 CAPLUS  
 DOCUMENT NUMBER: 1331835  
 TITLE: Preparation of 1-[3-(2,5-dioxopyrrolidino- or  
 2,6-dioxopiperidino)propyl]-4-arylpiperazines and  
 analogs as uroselective .alpha.1-adrenoceptor  
 antagonists  
 INVENTOR(S): Anand, Nitay; Sinha, Neelima; Jain, Sanjay; Mehta,  
 Anita; Bahadurupta, Jang  
 PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India  
 SOURCE: U.S., 10 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6083950	A	20000704	US 1998-120265	19980721
US 6090809	A	20000718	US 1998-203855	19981202
WO 200005206	A1	20000203	WO 1999-IB140	19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9919797 A1 20000214 AU 1999-19797 19990126 WO 200005205 A1 20000203 WO 1999-IB1296 19990716 V: AE, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9946410 A1 20000214 AU 1999-46410 19990716				

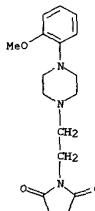
L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 BR 9912318 A 20010502 BR 1999-12318 19990716  
 EP 1097134 A1 20010509 EP 1999-929633 19990716  
 R: AT, BE, CH, DE, DK, ES, FR, GE, GR, IT, LI, LU, NL, SE, MC,  
 PT,  
 IE, SI, LT, LV, FI, RO  
 US 6410735 B1 20020625 US 2000-578088 20000524  
 US 6420366 B1 20020716 US 2000-57788 20000524  
 US 6420559 B1 20020716 US 2000-577789 20000524  
 PRIORITY APPLN. INFO.: IN 1997-DE3260 A 19971113  
 IN 1997-DE3261 A 19971113  
 US 1998-120265 A3 19980721  
 WO 1999-IB140 W 19990126  
 WO 1999-IB1296 W 19990716

OTHER SOURCE(S): MARPAT 133:89543  
 GI



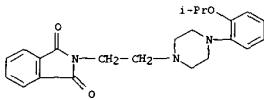
AB Title compds., e.g., R(CH<sub>2</sub>)<sub>n</sub>CHR3CH22R1 [I; R = 2,5-dioxopyrrolidino, 2,6-dioxopiperidino, etc.; R1 = (un)substituted 2-pyridinyl, -2-prymidinyl, -Ph; R3 = H, OH, alkyl, alkoxy; Z = piperidine- or piperazine-1,4-diy; n = 0-4] were prep'd. Thus, 2,5-dioxopyrrolidino was N-alkylated by 1-(3-chloropropyl)-4-(4-fluorophenyl)piperazine to give title compd. II. Data for biol. activity of I were given.  
 IT 255861-61-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPP (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USEs (Uses)  
 (prep. of 1-[3-(2,5-dioxopyrrolidino- or 2,6-dioxopiperidino)propyl]-4-arylpiperazines and analogs as uroselective .alpha.1-adrenoceptor antagonists)  
 RN 255861-61-1 CAPLUS  
 CN 2,5-Pyrrolidinedione,  
 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



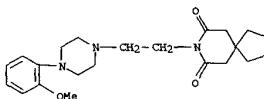
● HC1  
 REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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L14 ANSWER 33 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:379674 CAPLUS  
 DOCUMENT NUMBER: 133:150523  
 TITLE: Novel arylpiperazines as selective .alpha.1-adrenergic receptor antagonists  
 AUTHOR(S): Li, Xiaobing; Murray, William V.; Jolliffe, Linda;  
 Institute, Pulito, Virginia  
 CORPORATE SOURCE: The R. W. Johnson Pharmaceutical Research  
 San Diego, CA, 92121, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(10), 1093-1096  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A novel series of arylpiperazines has been synthesized and identified as antagonists of .alpha.1a adrenergic receptor (.alpha.1a-AR) implicated in benign prostatic hyperplasia. These compds. selectively bind to membrane bound .alpha.1a-AR with K<sub>i</sub>s as low as 0.66 nM. As such, these potentially represent a viable treatment for BPH without the side effects assoc'd with known .alpha.1-adrenergic antagonists.  
 IT 216252-67-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of arylpiperazines as selective .alpha.1-adrenergic receptor antagonists)  
 RN 216252-67-4 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-[4-[2-(1-methylethoxy)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

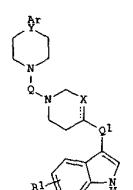
L14 ANSWER 34 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 results indicate that quant. pharmacol. can be studied successfully in single cells even though equil. could not be achieved in the agonist-antagonist-response relationship in this particular cell phenotype. The study also showed a form of fade that could be readily explained.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (single-cell recombinant pharmacol. of bovine .alpha.1a-adrenoceptor in rat fibroblasts and intracellular calcium release)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl  
 REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

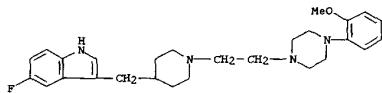
L14 ANSWER 34 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:373728 CAPLUS  
 DOCUMENT NUMBER: 133:84624  
 TITLE: Single-cell recombinant pharmacology: bovine .alpha.1a-adrenoceptors in rat-1 fibroblasts  
 release intracellular Ca<sup>2+</sup>, display subtype-characteristic agonism and antagonism, and exhibit an antagonist-reversible inverse concentration-response phase  
 AUTHOR(S): Pediani, John Daniel; Mackenzie, Janet Fraser; Heeley, Christie  
 CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience and Biomedical Systems, Institute of Biomedical Life Sciences, University of Glasgow, Glasgow, UK  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 887-895  
 CODEN: JPTAB1 ISSN: 0022-3565  
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Phenylephrine (Phe)-activated Ca<sup>2+</sup> signals recorded from single rat-1 fibroblasts stably expressing the bovine .alpha.1a-adrenoceptor (AR) were characterized and used to analyze functional agonist-antagonist interactions. The response to Phe was initiated by the mobilization of stored Ca<sup>2+</sup> and subsequently sustained by receptor-regulated Ca<sup>2+</sup> influx. The selective .alpha.1A-AR agonist (R)-A-61603 was 141-fold more potent than Phe. This potency ratio was consistent with the pharmacol. of the native .alpha.1A-ARs. Functional responses evoked by concns. of Phe of more than 0.3 .mu.M displayed fade, which could be explained by agonist-dependent depletion of Ca<sup>2+</sup> stores. The antagonists tested did not conform to the predictions of the Schild equation for competitive antagonism as expected from the nonequil. nature of the response. The antagonist potency series WB 4101 > toreg. prazosin > mchgt. BMY 7378, however, was consistent with .alpha.1A-ARs. Antagonism exhibited by WB 4101 and prazosin was compatible with a model in which antagonists dissociate so slowly from the receptor that this is a major factor in their inhibition of the transient agonist-mediated response, leading to the appearance of insurmountable antagonism. A consequence of this phenomenon was that an inverse concn.-response relationship at high agonist concns. was abolished by low concns. of antagonists. Overall, the

L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:345474 CAPLUS  
 DOCUMENT NUMBER: 132:347587  
 TITLE: Preparation of piperazinylalkylpiperidinyl(alkyl)iodide as serotoninergic agents.  
 INVENTOR(S): Kelly, Michael G.; Kang, Young H.  
 PATENT ASSIGNEE(S): American Home Products Corporation, USA  
 SOURCE: U.S., 6 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 US 6066637 A 20000523 US 1999-298202 19990423  
 PRIORITY APPLN. INFO.: MARPAT 132:347587  
 OTHER SOURCE(S): GI

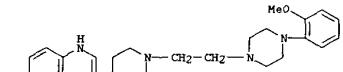


AB Title compds. [I]: R<sub>1</sub> = H, OH, OR<sub>2</sub>, F, Cl, Br, iod; R<sub>2</sub> = alkyl; Q = (CH<sub>2</sub>)<sub>m</sub>; Q<sub>1</sub> = (CH<sub>2</sub>)<sub>n</sub>; n = 0-2; X = CH, CH<sub>2</sub>; m = 2-4; Y = N, CH<sub>2</sub>; Ar = (substituted) aryl, heteroaryl, were prep'd. Thus, 4-(5-fluoro-1H-indol-3-ylmethoxy)piperidine, 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine, and X<sub>2</sub>C<sub>2</sub>O<sub>3</sub> were refluxed 5 h in MeCN to give 5-fluoro-3-[1-[2-(4-(2-methoxyphenyl)piperazin-1-yl)ethyl]piperidin-4-ylmethyl]-1H-indole. I displaced [3H]-paroxetine from serotonin transporters with K<sub>i</sub> = 1.2-19 nM.  
 IT 247911-01-9P 247911-02-0P 247911-05-3P  
 247911-06-4P 247911-07-5P 247911-08-6P  
 247911-09-7P 247911-12-2P 247911-14-4P  
 247911-15-5P 247911-16-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological)

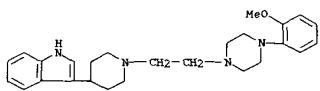
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prep. of piperazinylalkylpiperidinyl(alkyl)indoles as  
 serotoninergic agents)  
 RN 247911-01-9 CAPLUS  
 CN 1H-Indole,  
 5-fluoro-3-[(1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



RN 247911-02-0 CAPLUS  
 CN 1H-Indole,  
 5-fluoro-3-[(1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-piperidinyl)methyl]- (9CI) (CA INDEX NAME)

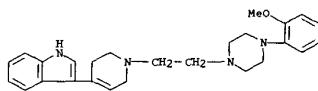


RN 247911-05-3 CAPLUS  
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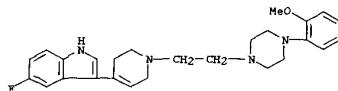


RN 247911-06-4 CAPLUS  
 CN 1H-Indole, 3-[(1,2,3,6-tetrahydro-1-{2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl}-4-pyridinyl)-4-pyridinyl]- (9CI) (CA INDEX NAME)

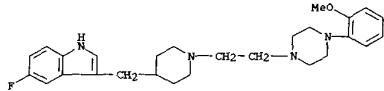
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 247911-07-5 CAPLUS  
 CN 1H-Indole, 5-fluoro-3-[(1,2,3,6-tetrahydro-1-{2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl}-4-pyridinyl)-4-pyridinyl]- (9CI) (CA INDEX NAME)



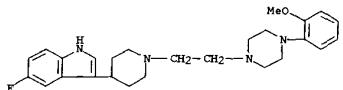
RN 247911-08-6 CAPLUS  
 CN 1H-Indole,  
 5-fluoro-3-[(1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-piperidinyl)methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 247911-09-7 CAPLUS  
 CN 1H-Indole,  
 5-fluoro-3-[(1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-piperidinyl)methyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

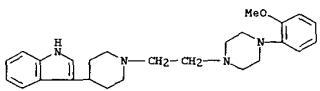


●2 HCl

RN 247911-12-2 CAPLUS  
 CN 1H-Indole, 3-[(1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-piperidinyl)methyl]-, (Z,E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

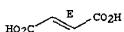
CRN 247911-05-3  
 CMF C26 H34 N4 O



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.

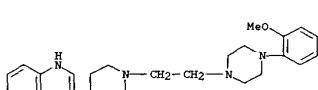


RN 247911-14-4 CAPLUS  
 CN 1H-Indole, 3-[(1,2,3,6-tetrahydro-1-{2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl}-4-pyridinyl)-4-pyridinyl]-, (Z,E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 247911-06-4  
 CMF C26 H32 N4 O

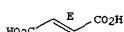
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CH 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

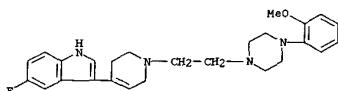
Double bond geometry as shown.



RN 247911-15-5 CAPLUS  
 CN 1H-Indole, 5-fluoro-3-[(1,2,3,6-tetrahydro-1-{2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl}-4-pyridinyl)-4-pyridinyl]-, (Z,E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

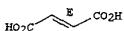
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 CMF C26 H31 F N4 O



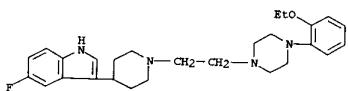
CH 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



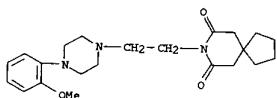
RN 247911-16-6 CAPLUS  
 CN 1H-Indole,  
 3-[1-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-4-piperidinyl]-  
 5-fluoro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L14 ANSWER 36 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:345446 CAPLUS  
 DOCUMENT NUMBER: 133:99703  
 TITLE: Cloning of rabbit .alpha.1b-adrenoceptor and  
 pharmacological comparison of .alpha.1a-,  
 .alpha.1b- and .alpha.1d-adrenoceptors in rabbit  
 AUTHOR(S): Piao, H.; Taniguchi, T.; Nakamura, S.; Zhu, J.;  
 Suzuki, F.; Mikami, D.; Muramatsu, I.  
 CORPORATE SOURCE: School of Medicine, Department of Pharmacology,  
 Fukui  
 Japan  
 SOURCE: Medical University, Matsukura, Fukui, 910-1193,  
 9-17 European Journal of Pharmacology (2000), 396(1),  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We have isolated a cDNA clone of the rabbit .alpha.1b-adrenoceptor  
 which has an open reading frame of 1557 nucleotides encoding a protein of  
 518 amino acids. The sequence shows higher identity to those of hamster,  
 human, and rat .alpha.1b-adrenoceptors than to those of rabbit  
 .alpha.1a- and .alpha.1d-adrenoceptors. The pharmacol. binding properties of  
 this clone expressed in Cos-7 cells showed a characteristic profile as  
 .alpha.1b-adrenoceptor; high affinity for prazosin ( $K_D=10.3$ ),  
 high affinity for tamsulosin (9.5) and low affinity for RMD 3213  
 (8.5), WB 4101 (8.7), and BMY 7378 (7.3). We have compared the levels of mRNA  
 expression of three .alpha.1-adrenoceptor subtypes in rabbit tissues  
 using the competitive reverse transcription/polymerase chain reaction  
 (RT/PCR) assay. In most rabbit tissues except heart, .alpha.1a-adrenoceptor  
 was expressed 10 folds more than the other two subtypes. However,  
 binding expts. with [ $^3$ H]prazosin and [ $^3$ H]RMD 3213 in rabbit tissues revealed a  
 poor relationship between binding d. and mRNA level. E.g., .alpha.1b  
 binding sites were exclusively predominant in spleen, whereas the  
 .alpha.1b subtype was minor at the mRNA level. These results  
 indicate a high identity of structural and pharmacol. profiles of three distinct  
 .alpha.1-adrenoceptor subtypes between rabbit and other species, but  
 there are species differences in their distribution.  
 IT 21102-95-4, RMY 7378  
 RL: BPR (Biological process); BSU (Biological study, unclassified);  
 BIOL (Biological study); PROC (Process)  
 (rabbit .alpha.1b-adrenoceptor sequence and expression and  
 pharmacol.)

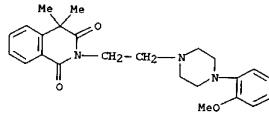
L14 ANSWER 36 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 comparison with other .alpha.1-adrenoceptor subtypes  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



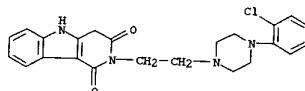
●2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE  
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L14 ANSWER 37 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:343282 CAPLUS  
 DOCUMENT NUMBER: 133:159627  
 TITLE: The ad hoc supermolecule approach to receptor  
 ligand  
 AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.;  
 Coccia, M.  
 CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena e  
 Reggio  
 SOURCE: Emilia, Modena, 41100, Italy  
 THEOCHEM (2000), 503(1-2), 1-16  
 PUBLISHER: CODEN: THEODJ; ISSN: 0166-1280  
 ELSEVIER SCIENCE B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Using the ligand design method based on the theor. QSAR paradigm, the  
 same ad hoc supermol. approach is presented and applied to a highly  
 non-congeneric set of .alpha.1-adrenergic receptor antagonists. The  
 performance of the approach is satisfactory and highlights its  
 (semi)quant. ligand design potentiality.  
 IT 67339-62-2 288073-32-3  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



RN 288073-22-3 CAPLUS  
 CN 1H-Pyrido[4,3-b]indole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-  
 piperazinyl]ethyl]-4,5-dihydro- (9CI) (CA INDEX NAME)



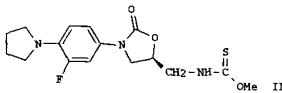
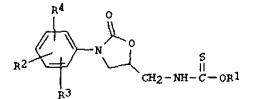
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR  
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L14 ANSWER 37 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:335397 CAPLUS  
DOCUMENT NUMBER: 132:334453  
TITLE: Preparation of oxazolidinylmethylthiocarbamic acid  
derivatives as antibacterial agents  
INVENTOR(S): Kado, Noriyuki; Tokuyama, Ryukou; Tsubouchi,  
Masatoshi; Tomita, Yayoi  
PATENT ASSIGNEE(S): Hokuriku Seiyaku Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 137 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

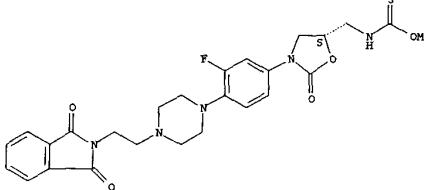
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027830	A1	20000518	WO 1999-JP6260	19991110
V: AE, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CR, CU, IL, MG, SL, BY, RW: DE, CF,	CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DK, ES, FI, FR, GE, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
JP 2000204084	A2	20000725	JP 1999-273230	19990927
EP 1130016	A1	20010905	EP 1999-971804	19991110
R: AT, BE, CH, DE, DK, ES, FR, GE, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO	AT, BE, CH, DE, DK, ES, FR, GE, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO	JP 1998-320137 A 19981111 JP 1999-273230 A 19990927 WO 1999-JP6260 W 19991110		
PRIORITY APPLN. INFO.:				
OTHER SOURCE(S): MARPAT 132:334453 GI				

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

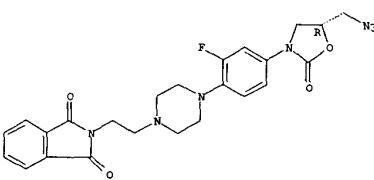


AB The title compds. I [R1 is optionally substituted alkyl or optionally substituted cycloalkyl; and R2, R3 and R4 are each independently hydroxyl, halogeno, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted amino, optionally substituted alkanoyl, optionally substituted cycloalkyloxy contg. a heteroatom as the ring-constituting atom, or an optionally substituted satd. heterocyclic group, or alternatively any two of R2, R3 and R4 together with the benzene ring may form an optionally substituted fused hydrocarbon ring] are prep'd. The title compd. II in vitro showed IC50 of 0.39 .mu.g/mL against S. aureus, vs. IC50 of 3.13 .mu.g/mL for linezolid.  
IT 268208-40-8P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(pred. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)  
RN 268208-40-8 CAPLUS  
CN Carbamothioic acid, [(5S)-3-[4-(4-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]-1-piperazinyl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]-, O-methyl ester (SCI) (CA INDEX NAME)  
Absolute stereochemistry. Rotation (-).

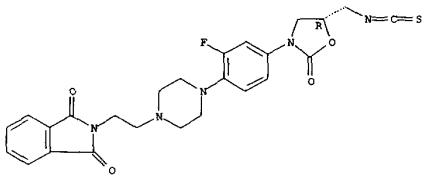
L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 268208-92-0P 268209-56-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(pred. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)  
RN 268208-92-0 CAPLUS  
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[(5R)-5-(azidomethyl)-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry. Rotation (-).



RN 268209-56-9 CAPLUS  
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[2-fluoro-4-[(5R)-5-(isothiocyanatomethyl)-2-oxo-3-oxazolidinyl]phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)  
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT.

AUTHOR(S): Makoto Shimamoto, Tetsuo Hayashi, Yasuhiro Nakaniishi, Kyoko Takiguchi, Chikako Oka, Naomi Inomata, Norio Suntory Institute for Biomedical Research, Osaka, 618-8510, Japan

CORPORATE SOURCE: Suntory Institute for Biomedical Research, Osaka, 618-8510, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(5), 623-635

CODEN: CPBTAL ISSN: 0009-2363

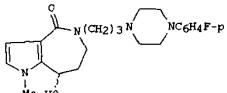
PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:104983

GI



I

AB A series of 5-aminoalkylpyrrolo[3,2-c]azepine derivs. was synthesized and their serotonin 2 (5-HT2) receptor antagonist and antiplatelet aggregation activities were evaluated. 5-HT2 receptor antagonist activity was largely detd. by the nature of the substituent at the 8-position as well as the aminoalkyl group at the 5-position of the pyrrolo[3,2-c]azepine ring. Compd. I was recognized as having potent 5-HT2 receptor antagonist activity with weak  $\alpha$ . $\beta$ . $\alpha$ . $\beta$ . adrenoceptor blocking activity and no significant D2 receptor binding affinity. (+)-I was resolved directly via diastereomeric salt formation and each enantiomer was evaluated. The 5-HT2 receptor antagonist activity of I was found to reside primarily in (-)-I ( $\alpha$ .OH) (which was about 14-fold more potent than (+)-I ( $\beta$ .OH) in isolated guinea pig arteries). Consequently, (S)-(-)-I (SUN CS174) displayed the overall best profile with potent 5-HT2 receptor antagonist activity ( $pA_2=8.98\pm0.06$ ) and high selectivity vs. other

platelet aggregation induced by serotonin in combination with collagen and ADP in canine or human platelet-rich plasma ( $IC_{50}=6.5$  to 16 nM). SUN CS174 significantly inhibited the mortality rate in mouse acute pulmonary thromboembolic death induced by collagen and serotonin at oral doses of 0.3 mg/kg or higher. SUN CS174 is currently undergoing clin. evaluation.

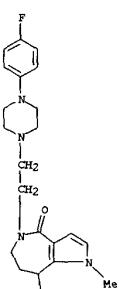
IT 191592-08-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (prep. and serotonin 2 (5-HT2) receptor antagonist activity of 5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related compds.)

RN 191592-08-2 CAPLUS

CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA INDEX NAME)

NAME



PAGE 1-A

PAGE 2-A

OH

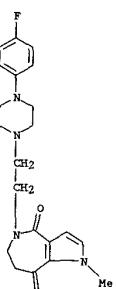
IT 191591-85-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prep. and serotonin 2 (5-HT2) receptor antagonist activity of 5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related compds.)

RN 191591-85-2 CAPLUS

CN Pyrrolo[3,2-c]azepine-4,8(1H,8H)-dione, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A



Me

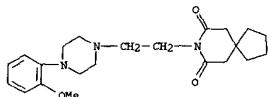
PAGE 2-A

REFERENCE COUNT: THIS

49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT.

L14 ANSWER 40 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:309881 CAPLUS  
 DOCUMENT NUMBER: 133:69131  
 TITLE: Splice isoforms of .alpha.1a-adrenoceptor in rabbit  
 AUTHOR(S): Suzuki, Fumiko; Taniguchi, Takanobu; Takaishi, Rumiko;  
 Corporate Source: Murata, Satoshi; Muramatsu, Ikunobu  
 Fukui Medical University, Fukui, 910-1193, Japan  
 SOURCE: British Journal of Pharmacology (2000), 129(8), 1569-1576  
 CODEN: BJPCM; ISSN: 0007-1188  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Two splice isoforms of rabbit .alpha.1a-adrenergic receptor (AR), (names)  
 .alpha.1a-OCU.2-AR and .alpha.1a-OCU.3-AR have been isolated from the liver cDNA library in addn. to the previously reported isoform (.alpha.1a-OCU.1-AR). Although they have the identical splice position with human .alpha.1a-AR isoforms, the C-terminal sequences are distinct from those of human isoforms. Among these rabbit .alpha.1a-AR isoforms, there are no significant differences in pharmacol. properties: high affinity for prazosin, WB 4101, XMD-3213 and YM 617 and low affinity for BMY 7378, using COS-7 cells expressing each isoform by radioligand binding assay. Competitive reverse transcription-polymerase chain reaction (RT-PCR) anal. revealed that mRNA of .alpha.1a-ARs was expressed in liver, thoracic aorta, brain stem and thalamus of rabbit. The splice isoforms exhibited a distinct distribution pattern in rabbit: .alpha.1a-OCU.1-AR was expressed most abundantly in those tissues. CHO clones, stably expressing each isoforms with receptor d. 740 fmol mg<sup>-1</sup> protein in .alpha.1a-OCU.1-AR, 1200 fmol mg<sup>-1</sup> in .alpha.1a-OCU.2-AR and 570 fmol mg<sup>-1</sup> in .alpha.1a-OCU.3-AR, resp., showed a norepinephrine-induced increase in inositol triphosphate which was suppressed by prazosin. Norepinephrine elicited a concn.-dependent increase in extracellular acidification rate (ECAR) in the CHO clones with pEC50 values of 6.19 for .alpha.1a-OCU.1-AR, 6.49 for .alpha.1a-OCU.2-AR and 6.58 for .alpha.1a-OCU.3-AR, resp. Norepinephrine caused a concn.-dependent increase in intracellular Ca<sup>2+</sup> concn. ([Ca<sup>2+</sup>]i) in the CHO clones with pEC50 values of 6.14 for .alpha.1a-OCU.1-AR, 7.25 for .alpha.1a-OCU.2-AR and 7.70 for .alpha.1a-OCU.3-AR, resp. In conclusion, the present study shows the occurrence of three splice isoforms of rabbit .alpha.1a-AR, which are

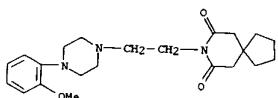
L14 ANSWER 40 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 unique in C-terminal sequence and in tissue distribution. They show similar pharmacol. profiles in binding studies but .alpha.1a-OCU.3-AR had the highest potency of norepinephrine in functional studies in spite of the lowest receptor d. These findings suggest that the structure of C-terminus of .alpha.1a-ARs may give the characteristic functional profile.  
 IT 21102-95-4, BMY 7378  
 RL: BPR (Biological process); BSU (Biological study, unclassified);  
 BIOL (Biological study); PROC (Process)  
 (.alpha.1a-adrenoceptor splice isoform sequence and functional expression and pharmacol. characterization in rabbit)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 41 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:273553 CAPLUS  
 DOCUMENT NUMBER: 133:13034  
 TITLE: .alpha.1-Adrenoceptor subtypes mediating contractions of the rat mesenteric artery  
 AUTHOR(S): Hussain, M. B.; Marshall, I.  
 Corporate Source: Department of Pharmacology, University College London, London, UK  
 SOURCE: European Journal of Pharmacology (2000), 395(1), 69-76  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The .alpha.1-adrenoceptor subtype(s) mediating contractions of the rat mesenteric artery were investigated using the agonists methoxamine, cirazoline, P 7480 and subtype-selective antagonists including BMY 7378. The pA2 or apparent pK<sub>B</sub> values of antagonists against methoxamine contractions correlated best with its pK<sub>B</sub> values at the cloned .alpha.1b-(0.88), with cirazoline, antagonists affinities correlated equally well with those at .alpha.1a-(0.79) or the .alpha.1b-(0.81) while with P 7480 antagonist affinities correlated best with the .alpha.1d-adrenoceptor subtype (0.94). The low affinity est. for 5-methylurapidil (7.3) against the .alpha.1a-selective cirazoline suggests an .alpha.1a-subtype mediating contraction is unlikely. Shallow Schild plot slopes of subtype selective antagonists against all three agonists are consistent with heterogeneity of .alpha.1-adrenoceptors. P 7480 (putative .alpha.1d-adrenoceptor-selective) acts primarily at this subtype and at another which is more likely to be an .alpha.1b- than an .alpha.1a-adrenoceptor. The results with both agonists and antagonists are consistent with contractions of the rat mesenteric artery being mediated via the .alpha.1d- and possibly .alpha.1b-adrenoceptor.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study); PROC (Process); BIOL (Biological study)  
 (.alpha.1-adrenoceptor subtypes mediating contractions of rat mesenteric artery and pharmacol. characterization thereof)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



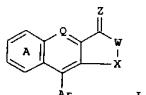
●2 HC1

REFERENCE COUNT:  
FOR THIS  
FORMAT

30 THERE ARE 30 CITED REFERENCES AVAILABLE  
RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 42 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:218572 CAPLUS  
DOCUMENT NUMBER: 132:260701  
TITLE: Tricyclic compounds, their preparation, and  
cyclic GMP  
INVENTOR(S): Tsuburai, Shigeru; Doi, Takayuki; Tarui, Naoki  
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 71 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

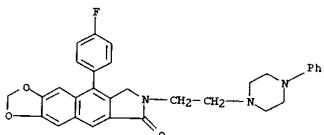
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000095759	A2	20000404	JP 1999-204103	19990719
PRIORITY APPLN. INFO.:			JP 1998-204963	19980721
OTHER SOURCE(S): MARPAT 132:260701 G1				



AB Title inhibitors contain tricyclic compds. I [ring A = (substituted) benzene ring; W = (substituted) NH; Q = CR, N; R = H, (substituted) alkyl, (substituted) alkoxy; X = (substituted) C1-2 alkylene; Z = H2, O; Ar = (substituted) arom. hydrocarbyl, (substituted) arom. heterocyclyl] or treated with BuLi followed by 2.3 g 4-FCGH4CN in THF/hexane at room temp. for 2 h and treated with 3.5 g maleimide and p-MeCGH4SO3H in PhMe under reflux for 15 h to give 5.6 g I [ring A = 1,3-benzodioxole, W = NH, Q = CH, X = CO, Z = O, Ar = CGH4F-p]. I [ring A = 1,3-benzodioxole, W = 4-pyridylmethylinino, Q = CH, X = CH2, Z = O, Ar = CGH4F-p] in vitro inhibited recombinant human phosphodiesterase with IC50 of 8.3 nM. Formulation examples are given.

IT 263018-67-3P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of tricyclic compds. as cyclic GMP phosphodiesterase

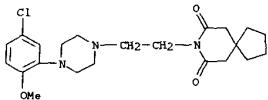
RN 263018-67-3 CAPLUS  
CN 6H-1,3-Benzodioxolo[5,6-f]isoindol-6-one,  
9-(4-fluorophenyl)-7,8-dihydro-7-[  
(2-(4-phenyl-1-piperazinyl)ethyl]- (SCI) (CA INDEX NAME)



L14 ANSWER 43 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:171777 CAPLUS  
DOCUMENT NUMBER: 132:303466  
TITLE: Effects of intracavernous administration of

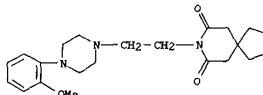
selective antagonists of .alpha.1-adrenoceptor subtypes on erection in anesthetized rats and dogs  
AUTHOR(S): Sironi, Giorgio; Colombo, Davide; Poggesi, Elena;  
Locardi, Amadeo; Testa, Rodolfo; Rampini, Olivier;  
Bernabe, Jacques; Giuliano, Francois  
CORPORATE SOURCE: Pharmaceutical R and D Division, Milan, Italy  
SOURCE: Therapeutics  
Therapeutics  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The proerectile properties of three novel .alpha.1-adrenoceptor (.-alpha.1-ADR) antagonists with different profiles of selectivity for the .alpha.1-ADR subtypes have been evaluated in anesthetized rats and dogs on intracavernous (IC) injection, in comparison with prazosin and phentolamine. In rats, the tested compds. decreased blood pressure (BP) and increased IC pressure (ICP), as well as the ratio ICP/BP. Rec 15/2841 (.alpha.1a- plus .alpha.1L-ADR-selective antagonist) and Rec 15/2615 (.alpha.1b-ADR selective) were the most potent compds. The ICP/BP ratios calc'd. after injection of Rec 15/3039 (.alpha.1d-ADR selective) were markedly different from those obsd. after vehicle injection. Prazosin and phentolamine proved poorly active, their main effect being hypotension. Approx. ED25 values (dose of compd. in micrograms inducing 25% ICP/BP ratio) were Rec 15/2615 (22 .mu.g/kg) > Rec 15/2841 (29 .mu.g/kg) > prazosin (136 .mu.g/kg) > phentolamine (1298 .mu.g/kg) > Rec 15/3039 (9600 .mu.g/kg). Submaximal stimulation of the cavernous nerve elicited an ICP rise whose amplitude was not altered by Rec compds. In contrast, prazosin and phentolamine decreased this ICP rise. All compds. but 15/3039 induced significant increase of the ICP/BP ratio in dogs. Rec 15/2615 proved to be the most interesting compd., inducing significant increases of ICP/BP at doses practically devoid of effects on BP. The rank order of potency in dog in increasing the ICP/BP ratio was similar to that obsd. in rats. Only at the highest doses tested, all compds., except Rec 15/3039, decreased the ICP rise elicited by submaximal stimulation of

L14 ANSWER 43 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
the cavernous nerve. Our data demonstrate that the .alpha.1b- and  
.alpha.1L-ADR subtypes are functionally relevant for the erectile  
function in these models, and that .alpha.1b- and/or .alpha.1L-ADR subtypes  
selective antagonists could represent a real advantage in erectile  
dysfunction therapy.  
IT 252240-56-5 REC 15/3039  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); BIOL (Biological study)  
(study, unclassified)  
(effects of intracavernous administration of selective  
antagonists of  
.alpha.1-adrenoceptor subtypes on erection in anesthetized rats  
and  
dogs)  
RN 252240-56-5 CAPLUS  
CN 8-Azaspiro[4.5]decano-7,9-dione,  
8-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

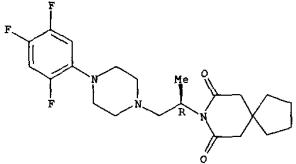
L14 ANSWER 44 OF 263 CAPLUS COPYRIGHT 2002 ACS  
(Continued)  
ACCESION NUMBER: 2000:125868 CAPLUS  
DOCUMENT NUMBER: 132:245855  
TITLE: Ligand design for .alpha.1-adrenoceptor subtype  
selective antagonists  
AUTHOR(S): Bremner, John B.; Cohen, Bursik; Griffith, Renate;  
Groenewoud, Karina M.; Yates, Brian P.  
CORPORATE SOURCE: Department of Chemistry, University of Wollongong,  
Wollongong, 2522, Australia  
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(1),  
201-214  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB In .alpha.1-Adrenoceptors there are three subtypes and drugs interacting  
selectively with these subtypes could be useful in the treatment of a  
variety of diseases. In order to gain an insight into the structural  
principles governing subtype selectivity, ligand based drug design  
(pharmacophore development) methods have been used to design a novel  
1,2,3-thiadiazole ring D analog of the aporphine system. Synthesis  
and  
testing of this compd. as a ligand on cloned and expressed human  
.alpha.1-adrenoceptors is described. Low binding affinity was found,  
possibly due to an unfavorable electrostatic potential distribution.  
Pharmacophore models for antagonists at the three adrenoceptor sites  
(.alpha.1A, .alpha.1B, .alpha.1D) were generated from a no. of  
different  
training sets and their value for the design of new selective  
antagonists  
discussed. The first preliminary antagonist pharmacophore model for  
the  
.alpha.1D adrenoceptor subtype is also reported.  
IT 23102-95-4 EMY-7378-3B-0, SNAP 8719  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological  
study, unclassified); BIOL (Biological study)  
(study, unclassified)  
antagonist  
RN 23102-95-4 CAPLUS  
CN 8-Azaspiro[4.5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

L14 ANSWER 44 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RN 255893-38-0 CAPLUS  
CN 8-Azaspiro[4.5]decano-7,9-dione, 8-[1(R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



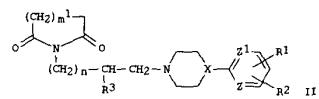
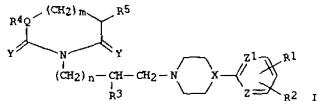
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESION NUMBER: 2000:84765 CAPLUS  
DOCUMENT NUMBER: 132:122634  
TITLE: Preparation of arylpiperazines as uro-selective  
.alpha.1-adrenoceptor blockers  
INVENTOR(S): Anand, Nituya; Sinha, Neelima; Jain, Sanjay; Mehta,  
Anita; Saxena, Anil Kumar; Gupta, Jang Bahadur  
PATENT ASSIGNEE(S): Rambaxy Laboratories Limited, India  
SOURCE: PCT Int. Appl., 59 pp.  
CODEN: PIXDZ2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005206	A1	20000203	WO 1999-1B140	19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, XZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CH, GA, GN, GW, ML, MR, NE, SN, TD, TG US 6003939 A 20000704 US 1998-120265 19980721 AU 991797 A1 20000214 AU 1999-19797 19990126 WO 2000005205 A1 20000203 WO 1999-1B1236 19990716 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9946410 A1 20000214 AU 1999-46410 19990716 BR 9912318 A 20010502 BR 1999-12318 19990716 EP 1097134 A1 20010509 EP 1999-929633 19990716 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 PRIORITY APPLN. INFO.: US 1998-120265 A 19980721  
 IN 1997-DE3260 A 19971113  
 IN 1997-DE3261 A 19971113  
 WO 1999-IB140 W 19990126  
 WO 1999-IB1296 W 19990716

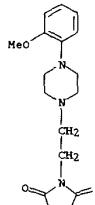
OTHER SOURCE(S): MARPAT 132:122634  
 G1



AB The title compds. [I; Y = O, S; Q, X, Z, and Z1 = CH, N; m = 0-3, n = 0-4; R1, R2 = H, F, Cl, etc.; R3 = H, R6, OH, OR6; R6 = alkyl; R4, R5 = alkyl, (un)substituted Ph, etc.] and more preferred compds. II [m1 = 1-4] which have been found to exhibit selective .alpha.1A adrenergic activity, were prepd. Thus, reacting 2,5-dioxopyrrolidine with 1-[4-(4-fluorophenyl)piperazin-1-yl]-3-chloropropane in the presence of K2CO3 and Bu4NBr in Me2CO afforded 65% II [m1 = 1; n = 1; X = N; Z = Z1 = CH; R1 = 4-F; R2 = R3 = H]. Biol. data for compds. II were given. The compds. I and II are useful for treatment of disease conditions, such as peripheral vascular disease, congestive heart failure, hypertension and esp. benign prostatic hypertrophy.

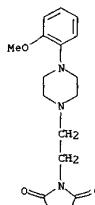
IT 255861-61-1P 255861-79-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of arylpiperazines as uro-selective .alpha.1-adrenoceptor

L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 blockers)  
 RN 255861-61-1 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HC1

RN 255861-79-1 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

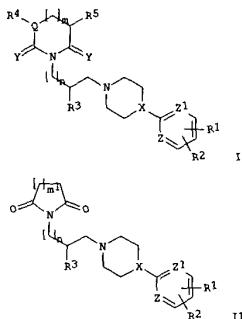
L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: WO 1999-1B1296 CAPLUS  
 DOCUMENT NUMBER: 132:107963  
 TITLE: Preparation of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers  
 INVENTOR(S): Anand, Nitay; Sinha, Neelima; Jain, Sanjay; Mehta, Anita; Saxena, Anil Kumar; Gupta, Jang Bahadur  
 PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India  
 SOURCE: PCT Int. Appl., 59 pp.  
 CODEN: PIXKD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005205	A1	20000203	WO 1999-1B1296	19990716
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, IS, JP, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, RU, TW, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6023950 A	20000704	US 1998-120265	19980721	
WO 2000005206	A1	20000203	WO 1999-IB140	19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946410 A1	20000214	AU 1999-46410	19990716	
BR 9912318 A	20010502	BR 1999-12318	19990716	
EP 1097134 A1	20010509	EP 1999-929633	19990716	
PT: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

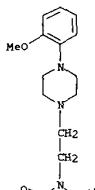
L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 IE, SI, LT, LV, FI, RO  
 JP 2002521362 T2 20020716 DE 2000-561162 19990716  
 PRIORITY APPLN. INFO.: US 1999-120365 A 19990721  
 WO 1999-1B140 V 19990726  
 IN 1997-DE3260 A 19971113  
 IN 1997-DE3261 A 19971113  
 IB 1999-IB9900140A 19990126  
 WO 1999-1B1296 W 19990716

OTHER SOURCE(S): MARPAT 132:107963  
 GI



AB The title compds. (I; Y = O, S; Q, X, Z, and Z1 = CH, N; m = 0-3, n = 0-4;  
 R1, R2 = H, F, Cl, etc.; R3 = H, R6, OH, OR6; R6 = alkyl; R4, R5 = H, alkyl, (un)substituted Ph, etc.) and more preferred compds. II [m] = 1-4] which have been found to exhibit selective .alpha.1A adrenergic activity.  
 Were prep'd. Thus, reacting 2,5-dioxopyrrolidine with 1-[4-(4-fluorophenyl)piperazin-1-yl]-3-chloropropane in the presence of K2CO3 and Bu4NBr in Me2CO afforded 65% II [m = 1; n = 1; X = N; Z = Z1 = CH; R1 = 4-F; R2 = R3 = H]. Biol. data for compds. II were given. The compds. I

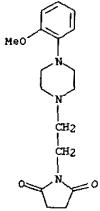
L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 and II are useful for treatment of disease conditions, such as peripheral vascular disease, congestive heart failure, hypertension and esp. benign prostatic hypertrophy.  
 IT 255861-61-1P 255861-79-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses) (prepns. of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers);  
 RN 255861-61-1 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HC1

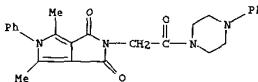
RN 255861-79-1 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



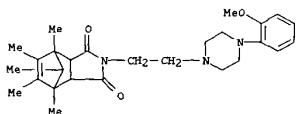
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 47 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000-74842 CAPLUS  
 DOCUMENT NUMBER: 132-224466  
 TITLE: Synthesis of some N-substituted 3,4-pyrroledicarboximides as potential CNS depressive agents  
 AUTHOR(S): Malinka, W.; Sieklucka-Dziuba, M.; Rajtar, G.; Rejdak, R.; Rejdak, K.; Klejnrok, Z.  
 CORPORATE SOURCE: Department of Chemistry of Drugs, Wroclaw Medical University, Lublin, Pol.  
 SOURCE: Phrazia (2000), 55(1), 9-16  
 PUBLISHER: PHARAT; ISSN: 0031-7144  
 PUBLISHER: Gori-Verlag Pharmazeutischer Verlag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Several novel N-substituted 3,4-pyrroledicarboximides were prep'd. and eleven representatives were examd. in a series of in vivo CNS tests.  
 A to that of 3,4-pyrroledicarboximides described previously; their structure-activity relationships are discussed.  
 IT 261164-81-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prep. of pyrroledicarboximides as potential CNS depressive agents);  
 RN 261164-81-2 CAPLUS  
 CN Piperazine, 1-{[3,5-dihydro-4,6-dimethyl-1,3-dioxo-5-phenylpyrrolo[3,4-c]pyrrol-2(H)-yl]acetyl}-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 48 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:74841 CAPLUS  
 DOCUMENT NUMBER: 132:222411  
 TITLE: Synthesis of new derivatives of 1,2,3,4,7-pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide with an expected anxiolytic activity  
 AUTHOR(S): Kossakowski, J.; Kusmierszky, J.  
 CORPORATE SOURCE: Department of Medical Chemistry, Medical University of Warsaw, Pol.  
 SOURCE: Pharmazie (2000), 55(1), 5-8  
 CODEN: PHARAT; ISSN: 0031-7144  
 PUBLISHER: Gova-Verlag Pharmazeutischer Verlag  
 DOCUMENT TYPE: Journal Article  
 LANGUAGE: English  
 AB: The prep. of a no. of derivs. of 1,2,3,4,7-pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide with potential anxiolytic activity has been described. The aim of our study was to obtain new analogs of tandospirone, that is derivs. of cyclic imides.  
 IT 261160-88-7P 261160-90-1P 261160-92-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); (prep., prep. and anxiolytic activity of pentamethylbicycloheptenedicarboximide).  
 RN 261160-88-7 CAPLUS  
 CN 4,7-Methano-1H-isindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,5,6,7,8-pentamethyl-, dihydrochloride (9CI) (CA INDEX NAME)



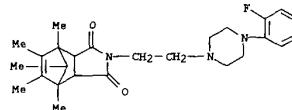
●2 HCl

RN 261160-90-1 CAPLUS  
 CN 4,7-Methano-1H-isindole-1,3(2H)-dione, 2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-4,5,6,7,8-pentamethyl-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:68449 CAPLUS  
 DOCUMENT NUMBER: 132:107961  
 TITLE: Preparation of 8-(2-piperazino(or piperidino)ethyl)-8-azaspiro[4.5]decane-7,9-diones as specific ligands for the human .alpha.1d adrenergic receptor  
 INVENTOR(S): Konkel, Michael; Wetzel, John M.; Noble, Stewart; Gluchowski, Charles; Craig, Douglas A.  
 PATENT ASSIGNEE(S): Synapse Pharmaceutical Corporation, USA  
 SOURCE: PCT Int. Appl., 97 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  

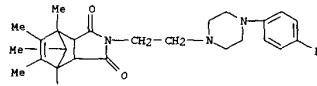
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004012	A1	20000127	WO 1999-US16101	19990716
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HV, ID, IL, IN, IS, JP, KE, KG, KP, KR, XZ, LC, LX, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SX, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9952146	A1	20000207	AU 1999-52146	19990716
EP 1100794	A1	20010523	EP 1999-937273	19990716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002050409	A2	20020709	JP 2000-560118	19990716
US 2002028760	A1	20020307	US 2001-764710	20010117
PRIORITY APPLN. INFO.: US 1999-118323	A2		US 1999-118323	19990717
OTHER SOURCE(S): MARPAT 132:107961			WO 1999-US16101	W 19990716

L14 ANSWER 48 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



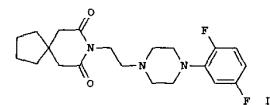
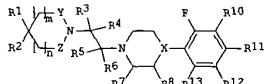
● HCl

RN 261160-92-3 CAPLUS  
 CN 4,7-Methano-1H-isindole-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-4,5,6,7,8-pentamethyl-, monohydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB: The title compds. [I; n = 0-2; m = 0-2; Y = CH2, CO, CS; Z = CH2, CO, R1, R2 = H, alkyl, alkoxy, etc.; R3 = H, alkyl, alkenyl, etc.; R4 = H, Me; R5 = H, alkyl, alkenyl, etc.; R6 = H, alkyl, alkenyl, etc.; R7 = H, alkyl, alkenyl, etc.; R8 = H, Me; R10 = H, F, Cl, etc.; R12 = H, F, Cl, etc.; R13 = H, F; X = N, CH] which binds selectively to a human .alpha.1d adrenergic receptor, and are useful in treating Raynaud's disease, and urinary incontinence, were prepd. and formulated.

Thus, heating 1-(2,5-difluorophenyl)piperazine with 8-(2-chloroethyl)-8-azaspiro[4.5]decane (preps. were given) afforded II which showed pKi of 9.0 at .alpha.1d receptor.

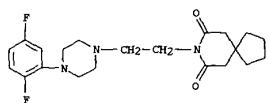
IT 255893-35-7P 255893-36-8P 255893-37-9P  
 255893-42-6P 255893-43-7P 255893-44-8P  
 255893-45-9P 255893-46-0P 255893-46-2P  
 255893-50-6P 255893-51-7P 255893-52-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

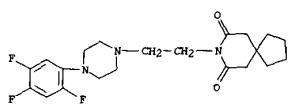
BIO (Biological study); PREP (Preparation); USES (Uses) (preps. of 8-(2-piperazino(or piperidino)ethyl)-8-azaspiro[4.5]decane-7,9-diones as specific ligands for the human .alpha.1d adrenergic receptor)

RN 255893-35-7 CAPLUS

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2,5-difluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

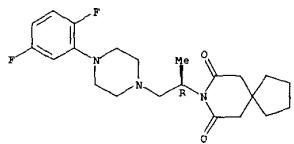


RN 255893-36-8 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2,4,5-trifluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 255893-37-9 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-2-[4-(2,5-difluorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

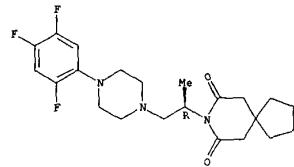
Absolute stereochemistry.



RN 255893-38-0 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

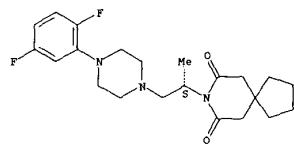
Absolute stereochemistry.

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



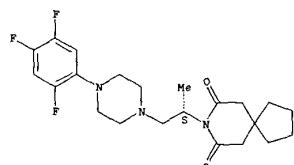
RN 255893-39-1 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1S)-2-[4-(2,5-difluorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

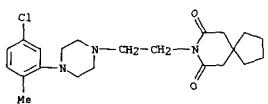


RN 255893-40-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1S)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

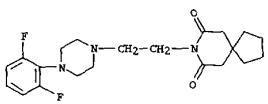
Absolute stereochemistry.



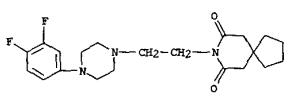
L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 255893-42-6 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(5-chloro-2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 255893-43-7 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2,6-difluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



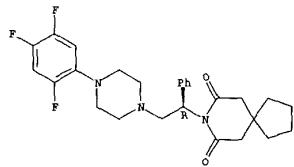
RN 255893-44-8 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(3,4-difluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 255893-45-9 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-phenyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

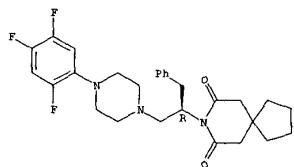
Absolute stereochemistry.

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

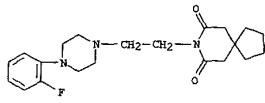


RN 255893-46-0 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-(phenylmethyl)-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

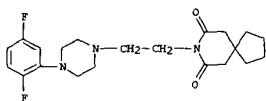
Absolute stereochemistry.



RN 255893-48-2 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-fluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

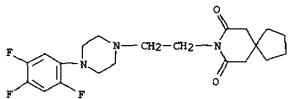


RN 255893-50-6 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2,5-difluorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

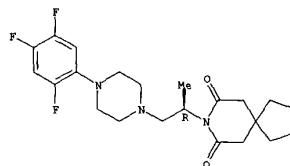
RN 255893-51-7 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2,4,5-trifluorophenyl)-1-piperazinyl)ethyl]-, hydrochloride (5:6) (CA INDEX NAME)



● 6/5 HCl

RN 255893-52-8 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-{4-(2,4,5-trifluorophenyl)-1-piperazinyl}ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

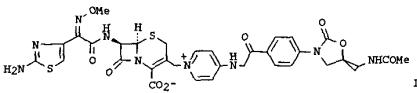
Absolute stereochemistry.



● HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:26717 CAPLUS  
 DOCUMENT NUMBER: 132:207679  
 TITLE: Synthesis and in vitro antibacterial activity of quaternary ammonium cephalosporin derivatives bearing oxazolidinone moiety  
 AUTHOR(S): Chung, In Hwa; Kim, Choong Sup; Seo, Jae Hong;  
 Chung, Bong Young  
 CORPORATE SOURCE: Biochemicals Research Center, Korea Institute of Science and Technology, Seoul, 130-650, S. Korea  
 SOURCE: Archives of Pharmacal Research (1999), 22(6), 579-584  
 CODEN: APHRDQ; ISSN: 0253-6269  
 PUBLISHER: Pharmaceutical Society of Korea  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB Several oxazolidinones having amine moiety were prep'd. to form a quaternary ammonium salt with cephalosporin nucleus, and antibacterial activity of the quaternary ammonium cephalosporin derivs. (e.g., I) bearing oxazolidinone moiety were exampd. particularly with expectation of enhanced antibacterial activity due to dual activity. However, the cephalosporin-oxazolidinone compds. revealed rather weaker antibacterial activity in vitro than their parent oxazolidinone and cephalosporin without showing any characteristic activity as expected.

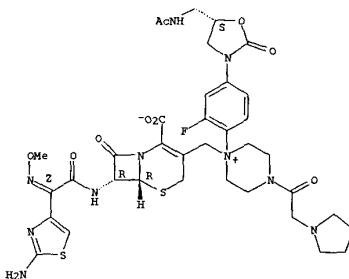
IT 260262-92-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis and antibacterial activity of quaternary ammonium oxazolidinonecephalosporin derivs.)  
 RN 260262-92-6 CAPLUS  
 CN Acetamide, N-[(5S)-3-[3-fluoro-4-(4-(1-pyrrolidinylacetyl)-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

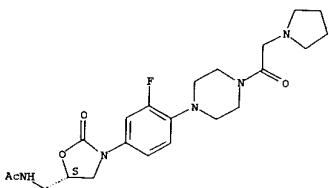
Chemical structure II: A complex molecule containing an oxazolidinone ring, a quaternary ammonium group, and a cephalosporin nucleus, similar to structure I but with different substituents.

L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 Absolute stereochemistry.  
 Double bond geometry as shown.



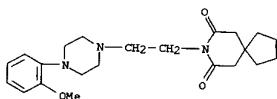
IT 260262-92-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis and antibacterial activity of quaternary ammonium oxazolidinonecephalosporin derivs.)  
 RN 260262-92-6 CAPLUS  
 CN Acetamide, N-[(5S)-3-[3-fluoro-4-(4-(1-pyrrolidinylacetyl)-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



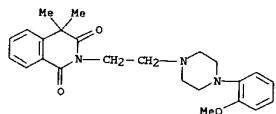
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 51 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:9434 CAPLUS  
DOCUMENT NUMBER: 132:146156  
TITLE: Relevance of theoretical molecular descriptors in quantitative structure-activity relationship analysis  
AUTHOR(S): of .alpha.1-adrenergic receptor antagonists  
Menziani, M. C.; Montorsi, M.; De Benedetti, P.  
Karelson, M.  
COPORATE SOURCE: Department of Chemistry, University of Modena and Reggio Emilia, Modena, 41100, Italy  
SOURCE: Bicorganic & Medicinal Chemistry (1999), 7(11), 2437-2451  
PUBLISHER: EMECEP; ISSN: 0968-0896  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A quant. structure-activity relationship (QSAR) study of a wide series of structurally diverse .alpha.1-adrenergic receptor antagonists was performed using the CODESSA (Comprehensive Descriptors for Structural and Statistical Anal.) technique. Theor. descriptors derived on a single structure and ad hoc defined size and shape descriptors were considered in the attempt of describing information relevant to receptor interaction. The relative effectiveness of these two classes of parameters in developing QSAR models for native (.alpha.1A and .alpha.1B) and cloned (.alpha.1a, .alpha.1b, and .alpha.1d) adrenergic receptor binding affinity, functional activity of vascular and lower urinary tract tissues, and in vitro and in vivo selectivity was evaluated.  
IT 21102-95-4, RMY 7378 67339-62-2, ARC 239  
99718-67-9  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (relevance of theor. mol. descriptors in QSAR anal. of .alpha.1-adrenergic receptor antagonists)  
RN 21102-95-4 CAPLUS  
CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

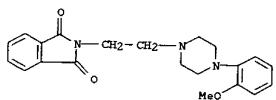


●2 HCl

RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-Isoquinolininedione, 2-[2-[(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

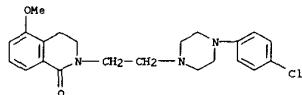


RN 99718-67-9 CAPLUS  
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

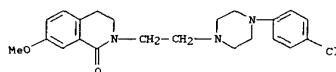


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

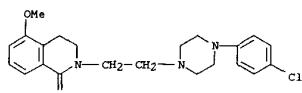
L14 ANSWER 52 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:815373 CAPLUS  
DOCUMENT NUMBER: 132:165762  
TITLE: A Structure-Affinity Relationship Study on Derivatives of N-[2-[(4-Chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide, a High-Affinity and Selective D4 Receptor Ligand  
AUTHOR(S): Perrone, Roberto; Berardi, Francesco; Colabufo, Nicola  
CORPORATE SOURCE: Dipartimento Farmaco-Chimico, Universita di Bari, Bari, 70126, Italy  
SOURCE: Journal of Medicinal Chemistry (2000), 43(2), 270-277  
PUBLISHER: JNCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: American Chemical Society  
LANGUAGE: Journal  
AB N-[2-[(4-Chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide, a high-affinity and selective dopamine D4 receptor ligand, was chosen as a lead, and structural modifications were done on its amide bond and on its alkyl chain linking the benzamide moiety to the piperazine ring and by prep. some semirigid analogs. The binding profile at dopamine D4 and dopamine D2, serotonin 5-HT1A, and adrenergic .alpha.1 receptors of 16 new compds. was detd. From the results emerged that the modification of the amide bond and the elongation of the intermediate alkyl chain caused a decrease in dopamine D4 receptor affinity. All prep'd. semirigid analogs displayed D4 receptor affinity values in the same range of the opened counterparts.  
IT 258882-65-4, 258882-66-5, 258882-78-9  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PRP (Preparation)  
[[(chlorophenyl)piperazin-1-yl]ethyl]methoxybenzamid e as selective D4 receptor ligand  
RN 258882-65-4 CAPLUS  
CN 1(2H)-Isoquinolinone, 2-[2-[(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-dihydro-5-methoxy- (9CI) (CA INDEX NAME)



RN 258992-66-5 CAPLUS  
CN 1(2H)-Isquinolinone,  
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-dihydro-5-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



RN 258992-79-9 CAPLUS  
CN 1(2H)-Isquinolinone,  
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-dihydro-5-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 53 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:805403 CAPLUS  
DOCUMENT NUMBER: 132:117709  
TITLE: Constitutive G12-dependent activation of adenylyl cyclase type II by the 5-HT1A receptor.

## Inhibition by

AUTHOR(S): Albert, Paul R.; Sajedi, Naghmeh; Lemonde, Sylvie; Ghahremani, Mohammad H.

CORPORATE SOURCE: National Research Institute, Departments of Medicine and Cellular and Molecular Medicine, University of Ottawa, Ottawa, ON, K1N 9M5, Can.

SOURCE: Journal of Biological Chemistry (1999), 274(50), 35469-35474

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The 5-HT1A receptor is implicated in depression and anxiety. This receptor couples to G<sub>i</sub> proteins to inhibit adenylyl cyclase (AC) activity but can stimulate AC in tissues (e.g., hippocampus) that express ACII. The role of ACII in receptor-mediated stimulation of cAMP formation was

examined in HEK-293 cells transfected with the 5-HT1A receptor, which displayed inhibition of basal and G<sub>s</sub>-induced cAMP formation in the absence

of ACII. In cells cotransfected with 5-HT1A receptor and ACII plasmids,

5-HT1A agonists induced a 1.5-fold increase in cAMP level.

Cotransfection of 5-HT1A receptor, ACII, and G. $\alpha$ .i2, but not G. $\alpha$ .i1,

G. $\alpha$ .i3, or G. $\alpha$ .o, resulted in an agonist-independent 6-fold increase in the basal cAMP level, suggesting that G<sub>i2</sub> preferentially coupled the

receptor to ACII. The 5-HT1B receptor also constitutively activated ACII. Constitutive activity of the 5-HT1A receptor was blocked by pertussis toxin and the G. $\beta$ . $\gamma$ . antagonist,  $\beta$ .CT, suggesting an important

role for G. $\beta$ . $\gamma$ -mediated activation of ACII. The Thr 149.fwdarw.

Ala mutation in the second intracellular domain of the 5-HT1A receptor disrupted G. $\beta$ . $\gamma$ -selective activation of ACII. Spontaneous

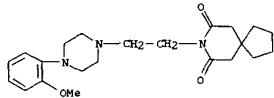
5-HT1A receptor activity was partially attenuated by 5-HT1A receptor partial agonists with anxiolytic activity (e.g., buspirone and flesinoxan) but was

not altered by full agonists or antagonists. Thus, anxiolytic activity may involve inhibition of spontaneous 5-HT1A receptor activity.

IT 21102-95-4, EMY-7378

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

L14 ANSWER 53 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
II by  
5-HT1A receptor and inhibition by anxiolytic partial agonists  
RN 21102-95-4 CAPLUS  
CN 8-Azapiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 54 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:750562 CAPLUS  
DOCUMENT NUMBER: 132:216950  
TITLE: Interaction of clozapine and other antipsychotic drugs

AUTHOR(S): Brooks, Karen M.; Cai, Jidong; Sandrasagra, Roehr, Joachim E.; Erraz, Rowena; Vargas, Hugo M. General Pharmacology, Hoechst Marion Roussel, Inc.,

CORPORATE SOURCE: Bridgewater, NJ, 08807-0800, USA Proceedings of the Western Pharmacology Society (1999), 42, 67-69

PUBLISHER: CODEN: PWPSA9; ISSN: 0083-8969 Western Pharmacology Society

DOCUMENT TYPE: Journal LANGUAGE: English

AB Antipsychotic drugs bind to a variety of neurotransmitter receptors. Blockade of brain  $\alpha$ .1-adrenergic receptors may contribute to the clin. efficacy and low extrapyramidal side effects of atypical antipsychotics. The authors evaluated clozapine and other antipsychotic drugs for interaction with human  $\alpha$ .1-adrenergic receptor subtypes.

The atypical antipsychotic drug clozapine demonstrated high affinity for each of the recombinant human  $\alpha$ .1-adrenergic receptors.

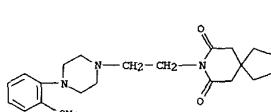
IT 21102-95-4, EMY 7378

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPP (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USMS (Uses)

(Interaction of clozapine and other antipsychotic drugs with human  $\alpha$ .1-adrenergic receptor subtypes)

RN 21102-95-4 CAPLUS

CN 8-Azapiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

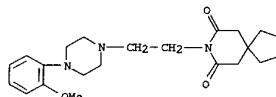


•2 HCl

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 54 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 55 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:750546 CAPLUS  
DOCUMENT NUMBER: 132:216777  
TITLE: Segmental differences in rat aorta contraction  
induced  
by phenylephrine in aortic rings  
AUTHOR(S): Asbun-Bojail, Juan; Escalante-Acosta, Bruno;  
Ceballos-Keyes, Guillermo; Ocharan-Hernandez,  
Maria  
Castillo-Henkel,  
Castillo-Henkel, Enrique F.;  
CORPORATE SOURCE: Carlos  
Seccion de Estudios de Posgrado e Investigacion,  
Escuela Superior de Medicina del Instituto  
Politecnico  
Nacional, Mexico, Mex.  
SOURCE: Proceedings of the Western Pharmacology Society  
(1999), 42, 23-24  
CODEN: PWPSAB; ISSN: 0083-8969  
PUBLISHER: Western Pharmacology Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB It was noted that vascular reactivity may differ between regions of  
the same vessel. The aim of the study was to evaluate the possibility of  
segmental differences in rat aorta contraction induced by  
phenylephrine.  
Concn.-response curves to phenylephrine obtained in thoracic and  
abdominal  
aortic rings with or without endothelium did not differ quant.  
IT 21102-95-4, RMY 7378  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(segmental differences in rat aorta contraction induced by  
phenylephrine)  
RN 21102-95-4 CAPLUS  
CN 8-Azapirro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

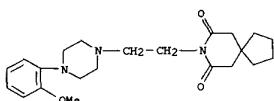
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L14 ANSWER 55 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 56 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:723048 CAPLUS  
DOCUMENT NUMBER: 131:346557  
TITLE: Method using .alpha.1D-adrenergic antagonists for  
treating bladder and lower urinary tract  
syndromes,  
and screening method  
INVENTOR(S): Schwinn, Debbie A.  
PATENT ASSIGNEE(S): Duke University, USA  
SOURCE: PCT Int. Appl., 38 pp.  
CODEN: PIXKD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957131	A1	19991111	WO 1999-US9846	19990506
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2327543	AA 19991111	CA 1999-2327543	19990506	
AU 9938830	A1	19991123	AU 1999-38830	19990506
EP 1075486	A1	20010214	EP 1999-921690	19990506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 2002513799	T2	20020514	JP 2000-547100	19990506
PRIORITY APPLN. INFO.: US 1998-84479P			US 1998-84479P	P 19980506
AB The invention relates to bladder and lower urinary tract syndromes, particularly, irritative symptoms, and to a method of treating them using an .alpha.1D-adrenergic receptor (.alpha.1DAR) antagonists. Also provided is a method of screening compds. for their ability to serve as .alpha.1DAR selective antagonists. IT 21102-95-4, RMY 7378 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES			WO 1999-US9846	W 19990506

L14 ANSWER 56 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (Uses) .alpha.1D-adrenergic antagonists for treating bladder and lower urinary tract syndromes, and screening method  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

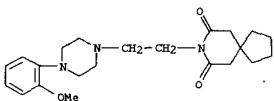


●2 HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

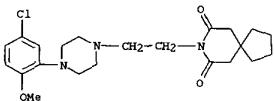
L14 ANSWER 57 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESION NUMBER: 1999:709584 CAPLUS  
 DOCUMENT NUMBER: 132:30785  
 TITLE: Inverse agonism and neutral antagonism at .alpha.1a- and .alpha.1b-adrenergic receptor subtypes  
 AUTHOR(S): Rossier, Olivier; Abuin, Liliane; Fanelli, Francesca; Leonardi, Amedeo; Cotecchia, Susanna  
 CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Universite de Lausanne, Lausanne, Switz.  
 SOURCE: Molecular Pharmacology (1999), 56(5), 858-866  
 CODEN: MOPMA3; ISSN: 0026-895X  
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics Journal  
 DOCUMENT TYPE: English  
 LANGUAGE: AB We have characterized the pharmacol. antagonism, i.e., neutral antagonism or inverse agonism, displayed by a no. of .alpha.-blockers at two .alpha.1-adrenergic receptor (AR) subtypes, .alpha.1a- and .alpha.1b-AR. Constitutively activating mutations were introduced into the .alpha.1b-AR at the position homologous to A293 of the .alpha.1b-AR where activating mutations were previously described. Twenty-four .alpha.-blockers differing in their chem. structures were initially tested for their effect on the agonist-independent inositol phosphate response mediated by the constitutively active A271E and A293E mutants expressed in COS-7 cells. A selected no. of drugs also were tested for their effect on the small, but measurable spontaneous activity of the wild-type .alpha.1a- and .alpha.1b-AR expressed in COS-7 cells. The results of our study demonstrate that a large no. of structurally different .alpha.-blockers display profound neg. efficacy at both the .alpha.1a- and .alpha.1b-AR subtypes. For other drugs, the neg. efficacy varied at the different constitutively active mutants. The most striking difference concerns a group of N-arylpiperazines, including 8-[2-(4-(5-chloro-2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4.5]decan-7,9-dione (REC 15/3039), REC 15/2739, and REC 15/3011, which are inverse agonists with profound neg. efficacy at the wild-type .alpha.1b-AR, but not at the .alpha.1a-AR.  
 IT 21102-95-4, RMY 7378 252240-56-5, REC 15/3039  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (inverse agonism and neutral antagonism at .alpha.1a- and .alpha.1b-adrenergic receptor subtypes)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-

L14 ANSWER 57 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

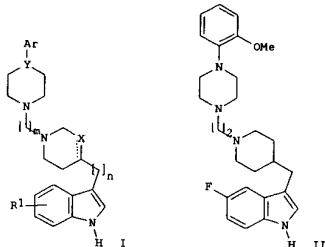
RN 252240-56-5 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione,  
 8-[2-(4-(5-chloro-2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



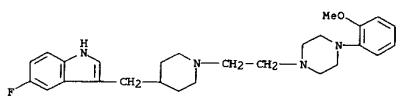
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 58 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESION NUMBER: 1999:709760 CAPLUS  
 DOCUMENT NUMBER: 131:310650  
 TITLE: Preparation of indolyl derivatives as serotonergic INVENTOR(S): Kelly, Michael Gerard; Kang, Young Hee  
 PATENT ASSIGNEE(S): American Home Products Corp., USA  
 SOURCE: PCT Int. Appl., 20 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  

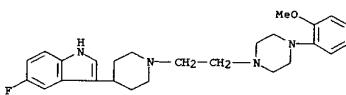
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955695	A1	19991104	WO 1999-US9181	19990428
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, XZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330437	AA	19991104	CA 1999-2330437	19990428
AU 9939670	A1	19991116	AU 1999-39670	19990428
EP 1073651	A1	19991207	EP 1999-922739	19990428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 20020513016	T2	20020508	JP 2000-545855	19990428
PRIORITY APPLN. INFO.: US 1998-69043			A 19980429	
OTHER SOURCE(S): MARPAT 131:310650			WO 1999-US9181	V 19990428
GI				



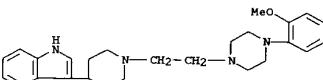
**AB lower** The title compd. [I; R1 = H, OH, OR2, halo (F, Cl, Br, I); R2 = alkyl; n = 0-2; X = CH, CH2; m = 2-4; Y = N, CH; Ar = (un)substituted aryl, heteroaryl] or their pharmaceutically acceptable salts, useful for the inhibition of serotonin uptake and the treatment of CNS disorders, particularly depression and anxiety. Thus, reaction of 4-(5-fluoro-1H-indol-3-ylmethyl)piperidine with 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine in the presence of K2CO3 and XI in MeCN afforded 80% II which showed Ki of 4.8 nM against [3H]-paroxetine binding. IT 247911-01-9P 247911-02-OP 247911-05-3P 247911-06-4P 247911-07-5P 247911-08-6P 247911-09-7P 247911-12-2P 247911-14-4P 247911-15-5P 247911-16-6P  
RLI-BN (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prep. of indolyl derivs. as serotonergic agents)  
RN 247911-01-9 CAPLUS  
CN 1H-Indole,  
5-fluoro-3-[(1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl)- (9CI) (CA INDEX NAME)



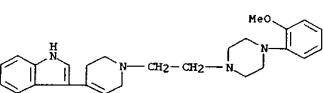
RN 247911-02-0 CAPLUS  
CN 1H-Indole,  
5-fluoro-3-[(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



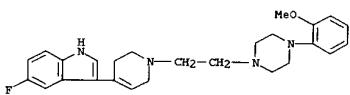
RN 247911-05-3 CAPLUS  
CN 1H-Indole, 3-[(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



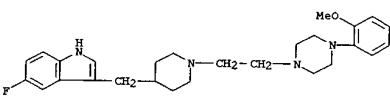
RN 247911-06-4 CAPLUS  
CN 1H-Indole, 3-[(1,2,3,6-tetrahydro-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)



RN 247911-07-5 CAPLUS  
CN 1H-Indole, 5-fluoro-3-[(1,2,3,6-tetrahydro-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)

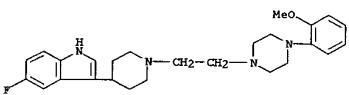


RN 247911-08-6 CAPLUS  
CN 1H-Indole,  
5-fluoro-3-[(1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl)methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 247911-09-7 CAPLUS  
CN 1H-Indole,  
5-fluoro-3-[(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

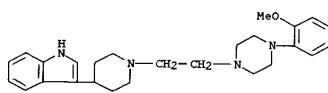


●2 HCl

RN 247911-12-2 CAPLUS  
CN 1H-Indole, 3-[(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-4-piperidinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

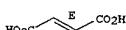
CRN 247911-05-3



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

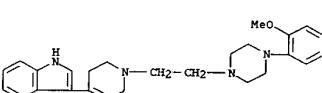
Double bond geometry as shown.



RN 247911-14-4 CAPLUS  
CN 1H-Indole, 3-[(1,2,3,6-tetrahydro-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-pyridinyl)-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

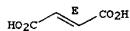
CRN 247911-06-4  
CMF C26 H32 N4 O



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

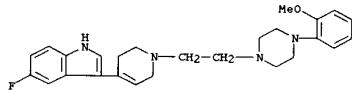
Double bond geometry as shown.



RN 247911-15-5 CAPLUS  
CN 1H-Indole,  
5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (1:2) (9CI)  
(CA INDEX NAME)

CM 1

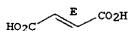
CRN 247911-07-5  
CMF C26 H31 F N4 O



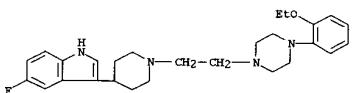
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



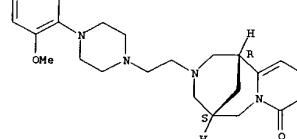
RN 247911-16-6 CAPLUS  
CN 1H-Indole,  
3-[1-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-  
5-fluoro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 59 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999;571555 CAPLUS  
DOCUMENT NUMBER: 131:337220  
TITLE: Synthesis and preliminary pharmacological evaluation  
of some cytisine derivatives  
AUTHOR(S): Boido, Caterina Canu Sparatore, Fabio  
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Genova, Genoa, 3-16132, Italy  
SOURCE: Farmaco (1999), 54(7), 438-451  
PUBLISHER: Elsevier Science S.A.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Thirty-one N-derivs. of cytisine were prep'd. to modify the pharmacol. profile and to obtain compds. of potential therapeutic interest either at a peripheral or central level, particularly as nicotinic ligands with improved ability to cross the blood-brain barrier. With the introduction of different kinds of substituents on the basic nitrogen of cytisine a variety of activities were obsd., both in vivo (analgesic, dopamine antagonism, antihypertensive, inhibition of stress-induced ulcers, antiinflammatory, protection from PAF-induced mortality, hypoglycemic) and *in vitro* (pos. cardio-inotropic, .beta.-adrenergic antagonism, .alpha.1- and .alpha.2-antagonism, inhibition of PAF-induced platelet aggregation). Six randomly selected compds. were tested for the ability to recognize a central nicotinic receptor and four of them exhibited Ki values in the range 30-163 nM.  
IT 249907-28-6  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepns. of cytisine derivs. and their preliminary pharmacol. evaluation)  
RN 249907-28-6 CAPLUS  
CN 1,5-Methano-8H-pyrido[1,2-a][1,5]diazocin-8-one, 1,2,3,4,5,6-hexahydro-3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride, (1R,5S)- (9CI) (CA INDEX NAME)

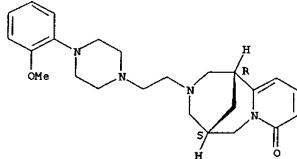
Absolute stereochemistry.



●2 HCl

IT 249906-94-3  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepns. of cytisine derivs. and their preliminary pharmacol. evaluation)  
RN 249906-94-3 CAPLUS  
CN 1,5-Methano-8H-pyrido[1,2-a][1,5]diazocin-8-one, 1,2,3,4,5,6-hexahydro-3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

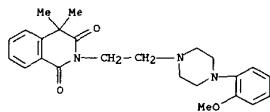
L14 ANSWER 60 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999/565907 CAPLUS  
DOCUMENT NUMBER: 131:194295.  
TITLE: Agents, and combinations thereof, with  
serotonin-related activity for the treatment of  
sleep-related breathing disorders  
INVENTOR(S): Radulovacki, Miodrag; Carley, David W.  
PATENT ASSIGNEE(S): The Board of Trustees of the University of  
Illinois,  
SOURCE: USA PCT Int. Appl., 46 pp.  
DOCUMENT TYPE: CODEN: PIKKD2  
LANGUAGE: Patent  
FAMILY ACC. NUM. COUNT: English 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943319	A1	19990902	WO 1999-USA3437	19990226
W: CA, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				
CA 2312900	AA	19990902	CA 1999-2312900	19990226
EP 1060636	A1	20010110	EP 1999-906636	19990226
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
JP 2002504510	T2	20020212	JP 2000-533116	19990226
US 6331535	B1	20011218	US 2000-6331535	20000923
US 2002086870	A1	20020704	US 2001-6001601	20011214
PRIORITY APPLN. INFO.:			US 1998-7621609	P 19980227
			WO 1999-USA3437	W 19990226
			US 2000-628238	A1 20000923

AB Pharmacol. methods are provided for the prevention or amelioration of sleep-related breathing disorders via administration of agents or combinations of agents that possess serotonin-related pharmacol. activity.  
 IT 67339-62-2, ARC239  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (agents, and combinations thereof, with serotonin-related activity for treatment of sleep-related breathing disorders)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isocoulinodiones, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 61 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999;547948 CAPLUS  
 DOCUMENT NUMBER: 131-281021  
 TITLE: Effect of several 5-hydroxytryptamineA receptor ligands on the micturition reflex in rats:  
 comparison with WAY 100635  
 AUTHOR(S): Testa, R.; Guarneri, L.; Poggesi, E.; Angelico, P.; Velasco, C.; Ibba, M.; Cilia, A.; Motta, G.  
 Riva, C.; Leonardi, A.  
 CORPORATE SOURCE: Pharmaceutical Research and Development Division, Milan, Italy  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics  
 (1999), 290(3), 1258-1269  
 PUBLISHER: CODEN: JPTETAB; ISSN: 0022-3565 American Society for Pharmacology and Experimental Therapeutics  
 DOCUMENT TYPE: Therapeutics  
 LANGUAGE: English  
 AB Several novel N-arylpiperazine derivs. were synthesized and tested for their (1) affinity and functional activity on 5-hydroxytryptamineA (5-HT1A) receptors in vitro; (2) activity in models predictive of antagonism at somatodendritic and postsynaptic 5-HT1A receptors; (3) and effects on the micturition reflex in anesthetized and conscious rats. The studies also included: 1-(2-methoxyphenyl)-4-(4-(2-phthalimidobutyl)piperazine hydrobromide (NAM 190), 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-aspiric[4,5]decane-7, 9-dione dihydrochloride (BMY 7378), and N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-(2-pyridinyl)cyclohexanecarboxamide (WAY 100635). Almost all compds. were found to be potent and selective for the human recombinant 5-HT1A receptor, with  $K_d$  values in the nanomolar range. [35S]GTP, $\gamma$ -gamma.S binding in HeLa cells expressing the recombinant human 5-HT1A receptor allowed classification of the compds. into neutral antagonists and partial agonists. Almost all neutral antagonists were active in blocking 8-hydroxy-2-dipropylaminotetralin (8-OH-DPAT)-induced forepaw treading in rats (postsynaptic model) and hypothermia in mice (somatodendritic model) with the same potency, whereas compds. showing partial agonistic activity were active in the postsynaptic model but were inactive, or poorly active, in the somatodendritic model. Neutral antagonists potently inhibited vol.-induced bladder-voiding contractions in anesthetized rats. Contractions were completely blocked, and the disappearance of bladder

L14 ANSWER 60 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

FORMAT

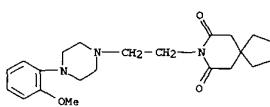
L14 ANSWER 61 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
contractions lasted 7 to 13 min after the highest doses tested.  
Furthermore, neutral antagonists increased bladder vol. capacity in  
conscious rats during continuous transvesical cystometry, whereas  
micturition pressure was only slightly, and not dose-dependently,  
reduced.

Partial agonists were inactive or poorly active, inducing a  
disappearance  
time of bladder contractions that did not exceed 6 min in anesthetized  
rats, and failing to increase bladder vol. capacity in conscious rats.  
These findings indicate that only neutral 5-HT1A receptor antagonists  
are endowed with inhibitory effects on the bladder.

IT 21102-95-4, BMY 7378  
RL: BAC (Biological activity or effector, except adverse); BPR  
(Biological  
process); BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study); FRCG (Process)  
(N-arylpiperazine derivs. affinity at 5-HT1A receptor and other G  
protein-coupled receptors and effects 5-HT1A receptor ligands on  
micturition reflex in rats)

RN 21102-95-4 CAPLUS

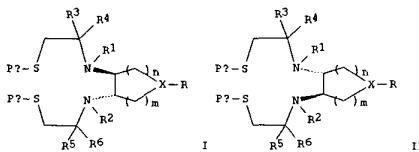
CN 8-Azaepi-4,5-dihydro-7,9-dione, 8-[2-(2-methoxyphenyl)-1-  
piperazinyl]heptyl-, dihydrochloride (9CI) (CA INDEX NAME)



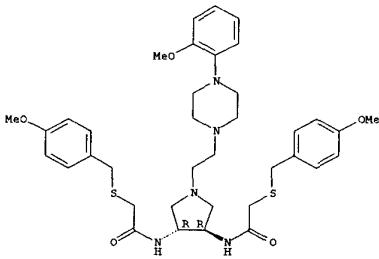
•2 HC1  
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999-528891 CAPLUS  
 DOCUMENT NUMBER: 131:153032  
 TITLE: Preparation of diaminedithiol stereoselective ligands to complex with technetium-99m pertechnetate for use as radiotracing agents  
 INVENTOR(S): Kung, Hank F.; Kung, Mei-ping; Zhuang, Zhi-ping  
 PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA  
 SOURCE: PCT Int. Appl., 58 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940882	A2	19990819	WO 1999-US2513	19990205
WO 9940882	A3	19991104		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, ES, FI, FR, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LZ, LK, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TH, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.: US 1998-73957P P 19980206			US 1998-78052P P 19980316	
OTHER SOURCE(S): MARPAT 131:153032				GI

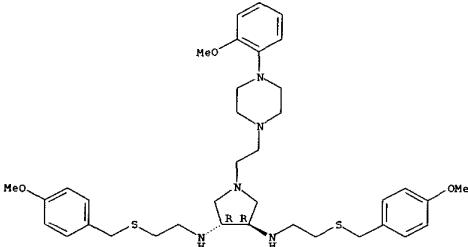


L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 235098-40-5 CAPLUS  
 CN 3,4-Pyrrolidinediamine,  
 N,N'-bis[2-[1-(4-methoxyphenyl)methyl]thio]ethyl]-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 235098-41-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)

L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB The present invention concerns novel diaminedithiol pyrrolidine deriv. ligands, represented by Formulas I and II, that form complexes with a radioactive metal through a chelate bond. The complexes are useful in radiodiagnostic compns. employed for imaging. In said ligand formulas, X  
 - N or CH, R1 and R2 are selected from H or (un)substituted alkyl or aralkyl where at least one of R1 and R2 is H, R3 and R4 are H or together form a keto group, R5 and R6 are H or together form a keto group, m and n are independently 1 or 2, R = H, (un)substituted C1-6 alkyl, C3-7 cycloalkyl, or C6-10ar(C1-4)alkyl, and Pa = sulfur protecting group or H. In addn., R in the formulas above may be -L-B where L is a linking group, e.g., alkyl, amido, hydrazino, etc., and B is a targeting group, e.g., amino acid, peptide, protein, antibody, nucleic acid, steroid, lipid, saccharide, or cell membrane ligand. Radionuclide complexes of I and II are claimed, e.g., with Tc-99m, Re-186, and Re-188. The compds. of the invention avoid the formation of diastereomer mixts. based on incorporating [TcVO]+3N2S2 as a chelating moiety since these compds. form only one isomer when complexed with [99mTcVO]4-. A process for radioimaging with the radionuclide complexes and a kit for forming an injectable radiopharmaceutical compn. contg. I and II are claimed. Examples are provided for the prepn. of the stereoselective ligands, e.g., (3R,4R)-I (X = N, R = PhCH2, Pa = R1 = R2 = R3 = R4 = H, n = m = 1), its radiolabeling with [99mTc]pertechnetate, and its biodistribution in rats, which showed good heart uptake. IT 235098-39-2P 235098-40-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (for prepn. of chiral diaminedithiol pyrrolidine deriv. as chelate ligand with radionuclides used as radioimaging agents)

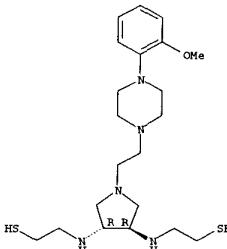
RN 235098-39-2 CAPLUS  
 CN Acetamide,  
 N,N'-[(3R,4R)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,4-pyrrolidinediyl]bis[2-[1-(4-methoxyphenyl)methyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (prepn. as chelate ligand with radionuclides used as radioimaging agents)

RN 235098-41-6 CAPLUS  
 CN Ethane-thiol,  
 2,2'-[{(3R,4R)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,4-pyrrolidinediyl}bis- (9CI) (CA INDEX NAME)

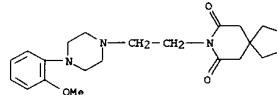
Absolute stereochemistry.



IT 235098-41-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)

L14 ANSWER 63 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:494795 CAPLUS  
 DOCUMENT NUMBER: 131:295533  
 TITLE: Importances of agonists in .alpha.-adrenoceptor classification and localization of .alpha.1-adrenoceptors in human prostate  
 AUTHOR(S): McGrath, J. C.; Naghadeh, M. A.; Pediani, J. D.; Mackenzie, J. F.; Daly, C. J.  
 CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neurosciences  
 Biomedical Sciences, and Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, G12  
 SOURCE: European Urology (1999), 36(Suppl. 1), 80-88  
 PUBLISHER: S. Karger AG  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB alpha-Adrenoceptor blocker drugs are commonly used in the clin. (non-surgical) treatment of BPH. .alpha.1-Adrenoceptors were originally sub-divided using agonists but, subsequently, were sub-divided using only antagonists in ligand-ligand interactions, which did not require all. Ultimately, proof that adrenoceptors are functional receptors for the natural ligands, noradrenaline and adrenaline, requires that agonists be used. The earlier excitement engendered by finding varying agonist potency series in different tissues has not been revisited to place it in the context of current concepts of .alpha.1-adrenoceptor subtypes. This review will consider the advantages and limitations of different agonists for the study of .alpha.1-adrenoceptor subtypes including "extreme" examples where the archetypal .alpha.1-adrenoceptor agonist phenylephrine activates .alpha.2-adrenoceptors and others where UK14304, often the .alpha.1-adrenoceptor agonist of choice, activates .alpha.1-adrenoceptors. New work will also be presented showing the interaction between agonists and the fluorescent .alpha.1-adrenoceptor antagonist QAPB. This introduces the novel point of view of studying the displacement of antagonists by agonists. Possible errors in antagonist classification arising from complexity in the actions of agonists and the recently developed method of fluorescent ligand binding on isolated living human prostatic smooth muscle cells will be discussed.  
 IT 21102-95-4, EMY7378  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological

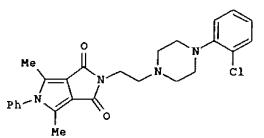
L14 ANSWER 63 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 process); BSU (Biological study, unclassified); BIOL (Biological study);  
 PROC (Process)  
 (importance of agonists in .alpha.-adrenoceptor classification and localization of .alpha.1-adrenoceptors in human prostate)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

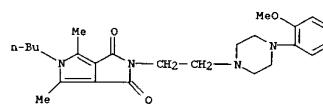
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:470679 CAPLUS  
 DOCUMENT NUMBER: 131:228607  
 TITLE: Synthesis and pharmacological screening of some N-(4-substituted-piperazin-1-ylalkyl)-3,4-pyrorolecarboximides  
 AUTHOR(S): Malinka, Wieslaw; Sieklucka-Dziuba, Maria; Rytar,  
 CORPORATE SOURCE: Grajyna; Rubaj, Andrzej; Kleinrok, Zdzislaw  
 Department of Chemistry of Drugs, Wroclaw  
 University of Medicine, Wroclaw, 50-137, Pol.  
 SOURCE: Farmaco (1999), 54(6), 390-401  
 PUBLISHER: Elsevier Science S.A.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 131:228607  
 GI

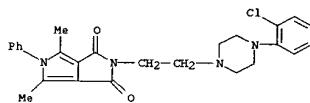


AB The synthesis and pharmacol. investigation of a new series of derivs. of pyrrole-3,4-dicarboximide, e.g. I, possessing the 4-substituted-piperazin-1-ylalkyl group linked to the imide nitrogen is presented. The products were evaluated for acute toxicity, and effectiveness in a series of CNS and arterial blood pressure tests. The preliminary pharmacol. screening was detd. in animal models. Several compds. demonstrated moderate to high analgesic activity in the "writhing syndrome" test (5f-1/640 LD50). Some of the structure-activity relationships are also discussed.  
 IT 244006-90-4P 244006-92-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (prepns. of piperazinylalkylpyrroledicarboximides with evaluation of depressant and analgesic activity)

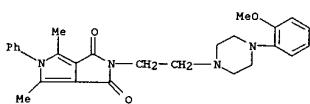
L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 244006-92-6 CAPLUS  
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



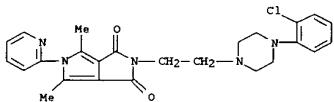
RN 244006-92-6 CAPLUS  
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



IT 244006-91-5P 244006-93-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. of piperazinylalkylpyrroledicarboximides with evaluation of depressant and analgesic activity)  
 RN 244006-91-5 CAPLUS  
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



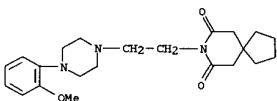
RN 244006-93-7 CAPLUS  
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 65 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:449795 CAPLUS  
DOCUMENT NUMBER: 131:223799  
TITLE: rabbit Analysis of  $\alpha$ .1-adrenoceptor subtypes in aorta and arteries: regional difference and co-existence  
AUTHOR(S): Sato, Mitsutoshi; Enomoto, Keisuke; Takayanagi, Issei; Koike, Katsuo  
CORPORATE SOURCE: University Department of Chemical Pharmacology, Toho School of Pharmaceutical Sciences, Funabashi, Japan European Journal of Pharmacology (1999), 374(2), 229-240  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB This study was done to det. the  $\alpha$ .1-adrenoceptor subtypes and to characterize the functional role of  $\alpha$ .1D-adrenoceptors in the following rabbit arteries: thoracic and abdominal aorta, mesenteric, renal, and iliac arteries. In all arteries, selective  $\alpha$ .1D-adrenoceptor antagonist BMY 7378 dose dependently shifted the concn.-response curves for norepinephrine to the right. Schild plots of the results obtained from the inhibition by BMY 7378 for norepinephrine yielded a straight line with a slope of unity in thoracic (pA2 6.54) and abdominal (pA2 6.73) aorta. Slopes of Schild plots obtained from the inhibition by BMY 7378 for norepinephrine were significantly different from unity in mesenteric, renal and iliac arteries. Slopes of Schild plots for BMY 7378 were not different from unity in chloroethylclonidine-treated thoracic (pA2 6.49) and abdominal (pA2 6.61) aorta. Slopes of Schild plots for BMY 7378 were significantly different from unity in chloroethylclonidine-treated mesenteric, renal and iliac arteries. On the other hand, in  $\text{Ca}^{2+}$ -free physiol. saline soln. ( $\text{Ca}^{2+}$ -free PSS) slopes obtained from Schild plots for BMY 7378 were not different from unity in thoracic (pA2 6.41) and abdominal (pA2 6.24) and iliac (pA2 6.64) arteries. BMY 7378 inhibited [ $^3\text{H}$ ]prazosin binding to thoracic (pKi 6.44) and abdominal (pKi 6.59) aorta with low potency, and mesenteric (pKi High 8.66, pKi Low 6.34), renal (pKi High 8.71, pKi Low 6.45) and iliac artery (pKi High 8.60, pKi Low 6.56). These results suggest that  $\alpha$ .1D-adrenoceptors play a significant role for contractile responses in renal and iliac artery, but play virtually no role in thoracic and abdominal aorta and that an  $\alpha$ .1-adrenoceptor subtype, which is pharmacol. distinguishable from the  $\alpha$ .1A,

L14 ANSWER 65 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
.alpha.1B- and .alpha.1D-adrenoceptor subtype, may co-exist in mesenteric artery.  
IT 21102-95-4, BMY 7378  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(.alpha.1-adrenoceptor subtype pharmacol. characterization in rabbit aorta and arteries and regional differences and co-existence therein)  
RN 21102-95-4 CAPLUS  
CN 8-Azapiro[4,5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

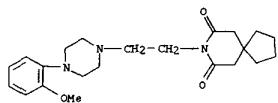


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REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 66 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:437513 CAPLUS  
DOCUMENT NUMBER: 131:194652  
TITLE: Microphysiometric analysis of human  $\alpha$ .1A-adrenoceptor expressed in Chinese hamster ovary cells  
AUTHOR(S): Taniguchi, Takachir Inagaki, Rika; Murata, Satoshi; Akiba, Isamu; Muramatsu, Ikuonobu  
CORPORATE SOURCE: Department of Pharmacology, Fukui Medical University, FUKUI, 910-1193, Japan  
SOURCE: British Journal of Pharmacology (1999), 127(4), 962-968  
PUBLISHER: Stockton Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The human recombinant  $\alpha$ .1A-adrenoceptor (AR) has been stably expressed in Chinese hamster ovary cells. Four stable clones, ah4, ah5, ah6 and ah7, expressing 30, 370, 940 and 2900 fmol AR mg<sup>-1</sup> protein, resp., have been employed to characterize this AR subtype using radioligand binding and microphysiometry to measure extracellular acidification rates. Noradrenaline (NA) gave concn.-dependent responses in microphysiometry with increasing extracellular acidification rates. The potency of NA increased as the receptor d. increased; pIC50 values of NA for the clones ah4, ah5, ah6 and ah7 were 6.9, 7.5, 7.8 and 8.1, resp. This increase of potency according to receptor d. indicates the presence of spare receptor for NA. Methoxamine, phenylephrine, oxymetazoline and clonidine also gave concn.-dependent responses with various intrinsic activities. Antagonists shifted concn.-response curves for NA rightward in a concn.-dependent manner. Schild anal. revealed that the affinity profile of this AR subtype to antagonists in the clone ah7 had a typical pattern for the  $\alpha$ .1A-AR; high affinity for prazosin and WB 4101, and low affinity for BMY 7378 (pA2=9.5, 9.8 and 7.3, resp.). This profile is similar in the case of the clone ah4. These affinities were in good agreement with those obtained in binding expts. These results have demonstrated that (1) classical receptor theory can be applied in microphysiometry, and (2) microphysiometry is a useful tool to investigate the pharmacol. characterization of  $\alpha$ .1A-AR.  
IT 21102-95-4, BMY 7378  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(microphysiometry in pharmacol. characterization of human

L14 ANSWER 66 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 .alpha.1a-Adrenoceptor expressed in Chinese hamster ovary cells  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

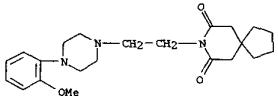


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REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 67 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 Characterization of .alpha.1-adrenoceptors expressed in a novel vascular smooth muscle cell line cloned from p53 knockout mice, P53IMAC01 (AC01) cells  
 AUTHOR(S): Ohma, Kazuhiko; Shinoura, Hitomi; Nakayama, Yasuhisa  
 CORPORATE SOURCE: Goda, Nobuhito; Tsujimoto, Gozo; Department of Pathology, National Children's Medical Research Center, Tokyo, 154-8509, Japan  
 SOURCE: British Journal of Pharmacology (1999), 127(3), 756-762  
 PUBLISHER: Stockton Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We pharmacol. studied the .alpha.1-adrenoceptor (AR) subtype(s) involved in receptor-mediated signaling in a novel vascular smooth muscle cell line cloned from p53 knockout mice, P53IMAC01 (AC01) cells. Radioligand binding studies with [<sup>3</sup>H]-HEAT showed the existence of a homogeneous population of binding site with an affinity (K<sub>d</sub> value) of 0.4 nM and a max. no. of binding sites (B<sub>max</sub>) of 100 fmol mg<sup>-1</sup> protein. Catecholamines competed for [<sup>3</sup>H]-HEAT binding stereospecifically and with the characteristic .alpha.1-AR potency series. Displacement curves for BMY-7378 and RMD-3213 best fitted a one-site model with a pK<sub>i</sub> value (-log<sub>10</sub> (equil. inhibition const.)) of 6.06 and 7.07, resp. Reverse transcription-polymerase chain reaction (RT-PCR) assay detected .alpha.1B, .alpha.1D, and .alpha.1A-AR, but not .alpha.1A-AR transcript. Chlorthalidone (CEC) treatment nearly abolished (-)noradrenaline (NA) (10 μM)-induced inositol[1,4,5]trisphosphate (IP<sub>3</sub>) prodn., and BMY-7378 inhibited the response with a K<sub>i</sub> value of 0.3 nM, which value was similar to that obtained in the cells expressing .alpha.1D-AR. In both AC01 cells and cells expressing .alpha.1D-AR, BMY-7378 protected .alpha.1-ARs from CEC alkylation while it had little protective effect on CEC alkylation and NA-induced IP<sub>3</sub> prodn. in cells expressing .alpha.1B-AR. The results indicate that AC01 cells contain predominantly .alpha.1B-ARs and a small population of .alpha.1D-ARs; however, phosphoinositide (PI)/Ca<sup>2+</sup> signaling is mainly mediated through the minor population of .alpha.1D-ARs, rather than the .alpha.1B-ARs.  
 IT 21102-95-4, BMY-7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (.alpha.1-adrenoceptor subtype functional pharmacol. characterization)

L14 ANSWER 67 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 and expression in vascular smooth muscle cell line cloned from p53 knockout mice  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

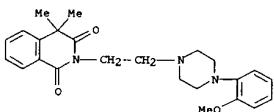


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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 68 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 Functional .alpha.2C-adrenoceptors in human neuroblastoma SH-SY5Y cells  
 AUTHOR(S): Parsley, Stephanie; Gazi, Lucien; Bobirian, Ionel; Loetscher, Erika; Schoeffter, Philippe  
 CORPORATE SOURCE: Nervous System Therapeutic Area, Novartis Pharma Research, Basel, CH-4002, Switz.  
 SOURCE: European Journal of Pharmacology (1999), 372(1), 109-115  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The .alpha.2-adrenoceptor mediating inhibition of forskolin-stimulated cAMP accumulation in human neuroblastoma SH-SY5Y cells was further characterized. The .alpha.2-adrenoceptor agonists, UK 14,304 (5-bromo-6-(2-imidazolin-1-yl)quinoxaline), oxymetazoline, guanfacine, (-)-noradrenaline and clonidine concn.-dependently decreased cAMP accumulation in this cell line (Emax apprx.50% inhibition). Agonist pEC50 values ranged between 6.7 and 7.8. Clonidine was a partial agonist. The effects of UK 14,304 were blocked after a pertussis toxin treatment. The concn.-response curves of UK 14,304 were shifted to the right in a parallel manner by the following antagonists (mean pK<sub>B</sub> values): yohimbine (8.17), idazoxan (7.63), prazosin (6.66), 2-[2-(4-(2-methoxyphenyl)piperazin-1-yl)ethyl]-4,4-dimethyl-1,3-(2H,4H) isoquinolindione (ARC 239; 7.12) and 2-(2,6-dimethoxyphenoxymethyl)aminomethyl-1,4-benzodioxane (WB-4101; 8.12). The relatively high pK<sub>B</sub> values of prazosin and ARC 239 point to a non-.alpha.2A-adrenoceptor-mediated effect. The relatively high pK<sub>B</sub> value of WB-4101 further characterizes the .alpha.2-adrenoceptor in SH-SY5Y cells as being of the .alpha.2C subtype. The anal. of the expression of .alpha.2-adrenoceptor subtypes by reverse transcriptase-polymerase chain reaction (RT-PCR) revealed the exclusive presence of .alpha.2C-adrenoceptor mRNA in SH-SY5Y cells. The authors propose that inhibition of forskolin-stimulated cAMP accumulation in SH-SY5Y cells be used as a functional model of human, native .alpha.2C-adrenoceptors.  
 IT 67339-62-2, ARC 239  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (.alpha.2C-adrenoceptors characterization in human neuroblastoma SH-SY5Y cell by .alpha.2-adrenoceptor agonist and antagonist)  
 RN 67339-62-2 CAPLUS  
 CN 1,3-(2H,4H)-Isoquinolindione, 2-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



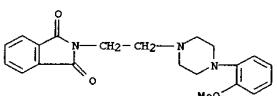
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:282212 CAPLUS  
DOCUMENT NUMBER: 130:311818  
TITLE: Preparation of arylpiperazines as serotonin reuptake inhibitors and 5-HT1D.alpha. antagonists  
INVENTOR(S): Walker, Clint Duane; Wong, David Taiwei; Xu, Yao-Chang  
PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
SOURCE: PCT Int. Appl., 61 pp.  
CODEN: PIXX02  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920621	A1	19990429	WO 1998-US2265	19981021
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RE: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2307114	AA	19980429	CA 19981021	
AU 9911931	AI	19980410	AU 19981021	
EP 1028958	AI	20000823	EP 1998-955031	19981021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2001520225	T2	20011030	JP 2000-516963	19981021
US 6342498	B1	20020129	US 2000-509957	20000331
PRIORITY APPLN. INFO.: US 1997-63493P			US 1997-63493P	P 19971022
OTHER SOURCE(S): MARPAT 130:311818			WO 1998-US2265	W 19981021
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*  
AB The title compds. [I: R1, R2 = H, halo, alkyl, etc.; R3 = H, alkyl; Y = CO, CH2; Z = NH, C(COR), CH2; R = alkyl, cycloalkyl; n, m = 1-3] and their salts, serotonin reuptake inhibitors and 5-HT1D.alpha. receptor

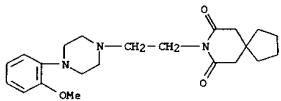
L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
antagonists useful in the treatment of depression and anxiety, were prepd. and formulated. E.g., a 4-step synthesis of piperazine II, starting with 1-(2-methoxyphenyl)piperazine, was given. Representative compds. I showed Ki at the 5-HT1A and 5-HT1D.alpha. receptors of at least 300 .mu.M. IT 99718-67-9# RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of arylpiperazines as serotonin reuptake inhibitors and 5-HT1D.alpha. antagonists)  
RN 99718-67-9 CAPTION  
CN 1H-Indoles-1,3(2H)-dione,  
2-(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 70 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:203816 CAPLUS  
DOCUMENT NUMBER: 131:27831  
TITLE: New .alpha.1-adrenoceptor antagonist, JTH-601, shows more than 10 times higher affinity for human prostates than arteries  
AUTHOR(S): Takahashi, Masahiko; Taniguchi, Takao; Murata, Satoshi; Okada, Kenichiro; Moriyama, Nobuo; Yamazaki, Satoru; Muramatsu, Ikuonobu  
CORPORATE SOURCE: Departments of Pharmacology and Urology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan  
SOURCE: Journal of Urology (Baltimore) (1999), 161(4), 1350-1354  
PUBLISHER: Lippincott Williams & Wilkins  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The authors compared the affinities of a new .alpha.1-adrenoceptor (AR) antagonist, JTH-601 with those of several .alpha.1-AR antagonists in human prostates and arteries. In the functional study, noradrenaline produced concen.-dependent contractions in human prostates and mesenteric arteries. The pA2/pKb values for the antagonists in the human prostate were 9.78 for tamsulosin, 8.84 for JTH-601, 8.39 for WB4101, 8.23 for prazosin, 8.12 for JTH-601-G1 (a main metabolite of JTH-601 in human) and 6.57 for BMY7378. Compared these affinities with those in the mesenteric artery, only JTH-601 and JTH-601-G1 exhibited unique uroselectivity, showing 10- to 20-fold higher affinity for the human prostate than for mesenteric artery. The affinity profile of these antagonists suggested that the noradrenaline induced contractions in the human prostate and the mesenteric artery were mediated by the .alpha.1A-AR and .alpha.1B-AR, resp. In the competition binding study, the pharmacol. profiles of the antagonists against [<sup>3</sup>H]-prazosin were examd. in the human prostate and aorta. The resulting pK<sub>B</sub> values for JTH-601 and JTH-601-G1 were also approx. 10- to 20-fold higher for the human prostate than for the human aorta. These results have suggested that JTH-601 and JTH-601-G1 are unique uroselective .alpha.1-AR antagonists that show higher affinity for the human prostate than for the human arteries.  
IT 2102-95-4, BMY7378  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological)

L14 ANSWER 70 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 study, unclassified); BIOL (Biological study)  
 (.alpha.1-adrenoceptor antagonist JTH-601 affinity comparison with  
 those of several .alpha.1-AR antagonists for human prostates and  
 arteries)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

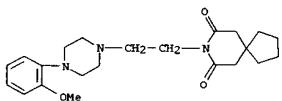


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REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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L14 ANSWER 71 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 study, unclassified); BIOL (Biological study)  
 (.alpha.1-adrenoceptor antagonist EMY-7378 in the rabbit thoracic aorta and iliac artery)  
 AUTHOR(S): Sato, Mitsuoshi; Enomoto, Keisuke; Takayanagi, Issei; Koike, Katsumi  
 CORPORATE SOURCE: Department of Chemical Pharmacology, Toho University  
 274-8510, School of Pharmaceutical Sciences, Chiba, Japan  
 SOURCE: Journal of Smooth Muscle Research (1998), 34(4), 151-158  
 PUBLISHER: Japanese Society of Smooth Muscle Research  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Based on the affinity of .alpha.1D-adrenoceptor subtype for a selective  
 antagonist EMY 7378, we studied its functional role in rabbit thoracic  
 aorta and iliac artery, and evaluated the subtypes of the  
 .alpha.1-adrenoceptors that are activated by phenylephrine (a full  
 agonist) and tizanidine (a partial agonist). In thoracic aorta, the  
 concn.-response curves of phenylephrine and tizanidine were  
 antagonized by  
 EMY 7378 with low potency (pA2 values 6.68+-0.06 and 6.67+-0.06,  
 slopes of Schild plot 1.06+-0.04 and 1.01+-0.04, resp.). On the  
 other hand, in iliac artery concn.-response curves for phenylephrine were  
 potently antagonized by a low concn. of EMY 7378, and the slope  
 (0.75+-0.02) of the Schild plot was significantly different from  
 unity.  
 In iliac artery, a concn.-response curve of tizanidine was  
 antagonized by  
 EMY 7378 with low potency (pA2 value 6.64+-0.08, slope of Schild  
 plot 1.01+-0.05). These results suggest that an .alpha.1D-adrenoceptor  
 subtype contributes to .alpha.1-adrenoceptor mediating muscle  
 contraction  
 in iliac artery, but not in thoracic aorta of rabbit, and that it is  
 activated by a full agonist phenylephrine but not by a partial agonist  
 tizanidine.  
 IT 21102-95-4, EMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BU  
 (Biological study, unclassified); BIOL (Biological study)  
 (antagonism difference for selective .alpha.1D-adrenoceptor  
 antagonists  
 EMY 7378 in thoracic aorta and iliac artery)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 71 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE  
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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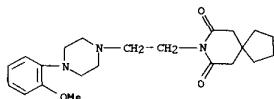
L14 ANSWER 72 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 study, unclassified); BIOL (Biological study)  
 Modification of sexual behavior of Long-Evans male rats by drugs acting on the 5-HT1A receptor  
 AUTHOR(S): Rehman, Jamil; Kaynan, Ayali; Christ, George;  
 Valcic, Mira; Maayani, Saul; Heiman, Arnold  
 CORPORATE SOURCE: Department of Urology, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, 10467,  
 USA  
 SOURCE: Brain Research (1999), 821(2), 414-425  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Modulation of the sexual behavior of male rats by the anxiolytic buspirone (8-  
 20499) and its analog gepirone were compared to the effects of  
 8-OH-DPAT (or DPAT, a selective 5-HT1A receptor agonist), and EMY-7378 (a  
 selective 5-HT1A partial agonist). Long-Evans rats were used;  
 modulation  
 of copulatory behavior and alteration of penile reflexes were examined.  
 Modulation of copulatory behavior was assessed by three indexes:  
 frequency  
 and length of intromission, and latency of ejaculation. DPAT, at  
 doses of  
 1-8 mg/kg, reduced these three indexes in a time dependent manner such  
 that the effects peaked at 45 min and normalized at 90 min. The  
 dose-effect relation (assessed 45 min after DPAT injection) is  
 bell-shaped  
 with an ED50 approx. 1 mg/kg on the ascending limb of the curve. The  
 effects of buspirone (2 mg/kg) and gepirone (2 mg/kg) on copulatory  
 behavior were indistinguishable from control. EMY-7378 alone and in  
 combination with these other 5-HT1A agonists reduced copulatory  
 behavior,  
 though not statistically significant. Penile reflexes, including no.  
 of  
 erections, cups and flips, were inhibited by these agents:  
 DPAT>buspirone>gepirone (inactive at 2 mg/kg). Furthermore, the  
 latency  
 period to erection was at least doubled by DPAT (2 mg/kg). Buspirone  
 and  
 gepirone, however, reduced the latency period to erection. EMY-7378  
 inhibited penile reflexes when administered alone and even more in  
 combination with DPAT or buspirone. Two butyrophenone analogs,  
 spiperone  
 (a 5-HT1A and dopamine D2 antagonist) and haloperidol (a D2  
 antagonist),  
 were also tested for their interaction with DPAT. Both of these  
 drugs (at  
 0.25 mg/kg, 60 min after administration) reduced all indexes of penile  
 reflexes and copulation. Furthermore, in combination with DPAT (2  
 mg/kg,  
 45 min), the effects were synergistic such that sexual activity came  
 nearly to a standstill. These opposing effects on putatively brain

L14 ANSWER 72 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 originated copulatory behavior and spinal mediated penile reflexes indicate that the effects of buspirone and DPAT on sexual behavior in the male rat may be possible at different parts of the central nervous system.

If a tentative shared target site by DPAT and buspirone is the 5-HT1A receptor, than the same 5-HT receptor sub-type at different locations (brain, raphe nuclei, spinal cord and autonomic ganglia) may modulate rat sexual behavior in opposing ways.

IT 21102-95-4, BMY-7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (modification of sexual behavior of Long-Evans male rats by drugs acting on the 5-HT1A receptor)

RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 73 OF 263 CAPLUS COPYRIGHT 2002 ACS 1999:120349 CAPLUS DOCUMENT NUMBER: 130:277169 TITLE: inverse agonists and phorbol myristate acetate in rat-1 fibroblasts stably expressing

.alpha.1d-adrenoceptors AUTHOR(S): Garcia-Sainz, J. Adolfo; Torres-Padilla, Maria Elena  
 CORPORATE SOURCE: Instituto de Fisiologia Celular, Universidad Nacinal

SOURCE: autonomia de Mexico, Mexico City, 04510, Mex.  
 FEBS Letters (1999), 443(3), 277-281

PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB In rat-1 fibroblasts stably expressing .alpha.1d-adrenoceptors, BMY 7378,

phentolamine, chloroethylclonidine and 5-methylurapidil decreased basal

[Ca2+]. WB 4101 induced a very small effect on this parameter but when added before the other antagonists it blocked their effect. All these agents inhibited the action of norepinephrine. Phorbol myristate acetate also blocked the effect of norepinephrine and decreased basal [Ca2+].

Staurosporin inhibited these effects of the phorbol ester. Our results suggest that: (1) .alpha.1d-adrenoceptors exhibit spontaneous ligand-independent activity, (2) BMY 7378, phentolamine,

chloroethylclonidine and 5-methylurapidil act as inverse agonists and

(3) protein kinase C activation blocks spontaneous and agonist-stimulated .alpha.1d-adrenoceptor activity.

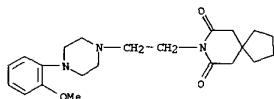
IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inverse agonist and protein kinase C modulation of intracellular calcium in rat-1 fibroblasts stably expressing .alpha.1d-adrenoceptors)

RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 73 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 74 OF 263 CAPLUS COPYRIGHT 2002 ACS 1999:69278 CAPLUS DOCUMENT NUMBER: 130:291449 TITLE: Affinity for both 5-HT1A- and D1-receptors and anxiolytic activity of N-(arylpiperazinylalkyl)-phthalimides

AUTHOR(S): Andronati, S. A.; Voronina, T. A.; Sava, V. M.; Molodavkin, G. M.; Makar, S. Yu.; Soboleva, S. G. A.V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, Odessa, 270080, Ukraine

SOURCE: Molecular Recognition and Inclusion, Proceedings of the International Symposium on Molecular

Recognition and Inclusion, 9th, Lyon, Sept. 7-12, 1996 (1998), Meeting Date 1996, 245-249. Editor(s): Coleman, Annette W. Kluwer: Dordrecht, Neth.

CODEN: 67FSAY  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

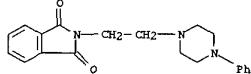
AB The authors report here affinity for both 5-HT1A- and D1-receptors and anxiolytic activity of N-(arylpiperazinylalkyl)-phthalimides.

IT 75000-24-7  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological processes); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(affinity for both 5-HT1A- and D1-receptors and anxiolytic activity of N-(arylpiperazinylalkyl)-phthalimides)

RN 75000-24-7 CAPLUS

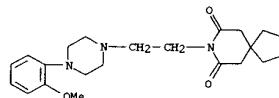
CN 1H-Isindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 75 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:55960 CAPLUS  
 DOCUMENT NUMBER: 130:262474  
 TITLE: Ultrasonic vocalizations in rat pups: effects of serotonergic ligands  
 AUTHOR(S): Olivier, B.; Molewijk, H. E.; Van Der Heyden, J.  
 A.  
 Miczek, K.  
 A.  
 CORPORATE SOURCE: Department of CNS Pharmacology, Solvay Pharmaceuticals, Weesp, 1380 DA, Neth.  
 SOURCE: Neuroscience and Biobehavioral Reviews (1998), 23(2), 215-227  
 PUBLISHER: CODEN: NBRDE; ISSN: 0149-7634  
 DOCUMENT TYPE: Elsevier Science Inc.  
 LANGUAGE: Journal English  
 AB Ligands with varying intrinsic activity and selectivity for the various subtypes of the serotonin receptor were tested in the rat pup ultrasonic vocalization (USV) model, a putative animal model reflecting anxiety. USV were elicited by isolating rat pups from their mother and littermates by placing them on a warm (37.degree.) or a cold (18.degree.) plate. Concurrently, the neg. geotactic (NG) response and rectal temp. were determined to assess the potentially sedative and hypothermic effects of putative anxiolytics. USV were reduced at low doses and in both temp. conditions by the full 5-HT1A receptor agonists flesinoxan and 8-OH-DPAT-HBr and the partial 5-HT1A receptor agonists buspirone, ipsapirone and BMY 7378. The 5-HT1A receptor antagonists NAN-190, (+)-WAY 100135, and (S)-UH-301 reduced USV at higher doses and only in one of both test conditions. The selective 5-HT1A receptor antagonist DU 125530 did not influence USV at the cold plate up to high doses, although concomitantly the neg. geotaxis was disturbed. The neg. geotaxis was impaired after all 5-HT1A receptor ligands, except BMY 7378 and (+)-WAY 100135. Hypothermia coincided with USV-suppression, except for NAN-190 and (S)-UH-301. The USV-suppressing action of flesinoxan (3 mg/kg) could be antagonized by DU 125530, but not its NG effect. However, the hypothermia induced by flesinoxan was antagonized by DU 125530. USV were also suppressed by the 5-HT uptake inhibitors fluvoxamine (both warm and cold plate) and

L14 ANSWER 75 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 clomipramine (only warm plate). The tricyclic antidepressant imipramine only decreased USV on the cold plate, however, in a U-shaped dose-response curve. At the highest dose tested, no decrease was present. The 5-HT uptake stimulant tianeptine reduced USV under both conditions. Fluvoxamine had no side effects, clomipramine induced hypothermia and tianeptine clearly had sedative properties. The 5-HT1B/2C receptor agonist TFMPP (trifluoromethylpiperazine) stimulated USV at a low dose at the cold plate and suppressed USV at a high dose under both conditions. The 5-HT2A/2C receptor antagonist ketanserin enhanced USV at low doses under both conditions and had no effect at a higher dose. Concurrently heavy sedation and hypothermia occurred. The 5-HT3 receptor agonist phenylbiguanide and the 5-HT3 receptor antagonist ondansetron had no effect in this paradigm. Clearly, subtypes of the 5-HT receptor affect rat pup USV differentially.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (serotonin receptor subtype ligand differential effect on ultrasonic vocalization in rat pup)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

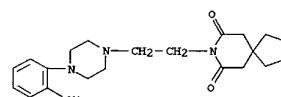


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REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 76 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:53147 CAPLUS  
 DOCUMENT NUMBER: 130:247299  
 TITLE: Characterization of 5-HT1A receptor functional coupling in cells expressing the human 5-HT1A receptor  
 AUTHOR(S): as assessed with the cytosensor microphysiometer  
 Dunlop, John; Zhang, Yingxin; Smith, Deborah L.; Schechter, Lee E.  
 CORPORATE SOURCE: Wyeth-Ayerst Research, CNS Disorders, Princeton, NJ,  
 SOURCE: 08543, USA  
 Methods: Journal of Pharmacological and Toxicological  
 (1998), 40(1), 47-55  
 PUBLISHER: CODEN: JPTHEZ; ISSN: 1056-8719  
 DOCUMENT TYPE: Elsevier Science Inc.  
 LANGUAGE: Journal English  
 AB The functional activity of a series of 5-HT1A receptor ligands has been evaluated in a cell line expressing the human 5-HT1A receptor (h5-HT1A .cndot. CHO) using the agonist-stimulated increase in extracellular acidification rate, measured with the microphysiometer, as a functional assay. Both 5-CT and 8-OH-DPAT were potent agonists in stimulating an increase in extracellular acidification rate in h5-HT1A .cndot. CHO cells with estd. EC50 values of 1.2 and 7.8 nM, resp. Addnl., these two 5-HT1A receptor agonists elicited a similar max. response. Concn.-dependent agonist activity was also obse. in the presence of buspirone, ipsapirone, BMY 7378, NAN-190 and WAY 100135, and each of these compds. behaved as partial 5-HT1A receptor agonists. The selective 5-HT1A receptor antagonist WAY 100635 produced a potent (IC50, 2.3 nM) and complete block of the 8-OH-DPAT-stimulated response. An evaluation of the inhibitory activity of a series of 5-HT1A receptor antagonists produced the following rank order of potency: WAY 100635 > LY 206130 (IC50, 7.1 nM) > WAY 100135 (30.8 nM) > pindolol (76.2 nM) > (-)-UH-301 (92.8 nM). Parallel studies on the inhibition of forskolin-stimulated adenylyl cyclase activity in h5-HT1A .cndot. CHO cells revealed that agonist potencies were generally similar between the two functional assays and were in good agreement with the estd. 5-HT1A receptor binding affinities. However, the relative efficacies detd. for the partial agonists in the cAMP assay were substantially greater than those obse. with the microphysiometer. Finally, antagonists were considerably weaker in the cAMP assay compared

L14 ANSWER 76 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 with the microphysiometer. The evaluation of 5-HT1A ligands using the microphysiometer, which represents a very distinct indice of 5-HT1A receptor function compared with the cAMP assay, results in a different profile of functional activity.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (5-HT1A receptor functional coupling characterization in cells expressing the human 5-HT1A receptor as assessed by extracellular acidification rate detn. with the cytosensor microphysiometer and cAMP formation)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

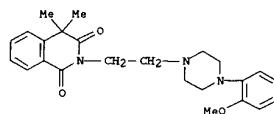


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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 77 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999-32567 CAPLUS  
 DOCUMENT NUMBER: 130:765 CAPLUS  
 TITLE: Role of the third intracellular loop of the  
 alpha-2  
 adrenergic receptor in regulating receptor  
 density  
 AUTHOR(S): Heck, Donald A.; Bylund, David B.  
 CORPORATE SOURCE: Dep. Pharmacology, Medical Center, Univ.  
 Nebraska,  
 SOURCE: Omaha, NE, 68198, USA  
*Pharmacology Reviews and Communications* (1998),  
 10(2), 101-110  
 PUBLISHER: CORP: PHRCF6  
 DOCUMENT TYPE: Harwood Academic Publishers  
 LANGUAGE: English  
 AB It was previously shown that the mechanism of down-regulation of  
 .alpha.-2  
 adrenergic receptor subtypes is an increase in the rate const. for  
 receptor disappearance. In addn., subtype-specific differences were  
 found  
 in the regulation of receptor d. in the presence of norepinephrine.  
 For  
 example, blocking functional G protein coupling with pertussis toxin  
 alters the time-course of norepinephrine-induced down-regulation for  
 .alpha.-2A receptors while having little effect on the time-course of  
 receptor down-regulation for .alpha.-2B receptors. In contrast,  
 treatment  
 with pertussis toxin alone decreases .alpha.-2B receptor d. while  
 having  
 little effect on .alpha.-2A receptor d. To explore these  
 subtype-specific  
 differences, a chimeric receptor was constructed in which the 3rd  
 intracellular loop of the .alpha.-2B receptor was replaced with the  
 3rd  
 intracellular loop of the .alpha.-2A receptor. It was found that the  
 chimeric receptor exhibits similar characteristics to the wild-type  
 receptor in terms of radioligand binding, potency of norepinephrine  
 to  
 down-regulate receptor d., and effects of pertussis toxin on  
 receptor d.  
 In contrast, replacement of the 3rd intracellular loop of the  
 .alpha.-2B  
 receptor with that of the .alpha.-2A receptor alters the regulation  
 of  
 receptor d. in both the absence and presence of norepinephrine.  
 IT 67339-62-2, ARC-239  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); BIOL (Biological study)  
 (affinity for .alpha.-2 adrenergic receptors and chimeric  
 receptor)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolininedione, 2-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

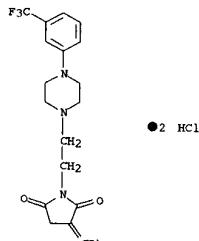
L14 ANSWER 77 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR  
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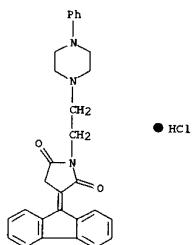
L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 ACCESSION NUMBER: 1998-804630 CAPLUS  
 DOCUMENT NUMBER: 130:191412 CAPLUS  
 TITLE: Synthesis and Structure-Activity Relationships  
 of a  
 New Model of Arylpiperazines. 4-1-.omega.-(4-  
 Arylpiperazin-1-yl)alkyl-3-(diphenylmethylene)-  
 2,5-pyrrolidinediones and  
 -3-(9H-fluoren-9-ylidene)-  
 2,5-pyrrolidinediones: Study of the Steric  
 Requirements of the Terminal Amide Fragment on  
 5-HT1A  
 AUTHOR(S): Affinity/Selectivity  
 Lopez-Rodriguez, Maria L.; Morcillo, M. Jose;  
 Rovat,  
 Tandu K.; Fernandez, Esther; Vicente, Bruno;  
 Sanz,  
 Antonio M.; Hernandez, Medardo; Orensan, Luis  
 CORPORATE SOURCE: Departamento de Quimica Organica I Facultad de  
 Ciencias Quimicas, Universidad Complutense,  
 Madrid,  
 SOURCE: 28040, Spain  
*Journal of Medicinal Chemistry* (1999), 42(1),  
 36-49  
 PUBLISHER: CODEN: JMCAR; ISSN: 0022-2623  
 DOCUMENT TYPE: American Chemical Society  
 LANGUAGE: Journal  
 OTHER SOURCE(S): English  
 AB In the present paper, the authors report the synthesis and the  
 binding  
 profile on 5-HT1A, .alpha.1 and D2 receptors of a new series of  
 1-[.omega.-(4-arylpiperazin-1-yl)alkyl]-3-(diphenylmethylene)-2,5-  
 pyrrolidinediones (I) (1-4) and -3-(9H-fluoren-9-ylidene)-2,5-  
 pyrrolidinediones (II) (1-4), in which the aryl linker contains 1-4  
 methylenes and the aryl group is variously substituted. The results  
 obtained are compared to those previously reported for  
 bicyclohydantoin  
 and the related bicyclic amine series. A considerable part of the  
 tested  
 compds. demonstrated moderate to high affinity for 5-HT1A and  
 .alpha.1  
 receptor binding sites but had no affinity for D2 receptors. The  
 study of  
 the length of the alkyl chain and the imide substructure has allowed  
 the  
 authors to suggest some differences between the 5-HT1A and the  
 .alpha.1-adrenergic receptors: (i) for I and II, affinity for the  
 5-HT1A  
 receptor as a function of the length of the methylene linker  
 decreases in  
 the order >1 .mchgt. 3.apprx.2, while for the .alpha.1 receptor  
 affinity  
 decreases in the order 3.apprx.4 > 1.apprx.2; (ii) the  
 non-pharmacophoric  
 steric pocket (receptor zone which does not hold the pharmacophore  
 of the

L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 ligand but holds a nonessential fragment of the mol.) in the 5-HT1A  
 receptor has less restriction than the corresponding pocket in the  
 .alpha.1-receptor. Compds. which are highly selective for  
 .alpha.1-adrenergic receptors displayed antagonist activity. The best  
 compromise between affinity and selectivity for 5-HT1A receptors is  
 reached in these new series with n = 1, which is in agreement with the  
 authors previous results for the bicyclohydantoin derivs. Two  
 selected  
 compds. retain agonist properties at postsynaptic 5-HT1A receptors.  
 The  
 same 5-HT1A agonist profile found in these compds. suggests the  
 existence  
 of two different non-pharmacophoric steric pockets in this receptor  
 and a  
 different interaction of compds. with n = 1 and n = 4. The  
 information  
 obtained from the interpretation of the energy minimization and  
 2D-NOESY  
 expts. of these compds. together with the synthesis and binding data  
 of  
 new conformationally restrained analogs is in good agreement with this  
 working hypothesis.  
 IT 220798-79-8  
 RL: BPR (Biological process); BSU (Biological study, unclassified);  
 PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study);  
 PREP (Preparation); PROC (Process)  
 (synthesis and structure-activity relationships of a new model of  
 arylpiperazines and study of steric requirements of terminal amide  
 fragment on 5-HT1A affinity/selectivity in relation to  
 .alpha.1-adrenergic and D2 receptors)  
 RN 220798-79-8 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-[3-  
 (trifluoromethyl)phenyl]-1-piperazinyl)ethyl]-, dihydrochloride (9CI)  
 (CA  
 INDEX NAME)

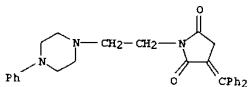


IT 193287-12-6P 193287-13-7P 193287-15-9P  
193287-16-0P 193287-18-2P 193287-19-3P  
220798-76-5P 220798-85-6P 220798-90-3P  
RL: BPR (Biological process); BSU (Biological study, unclassified);  
SPN (Synthetic preparation); BIOL (Biological study); PREP  
(Preparation); PROC  
(Process)  
(synthesis and structure-activity relationships of a new model of arylpiperazines and study of steric requirements of terminal amide fragment on 5-HT1A affinity/selectivity in relation to alpha.1-adrenergic and D2 receptors)

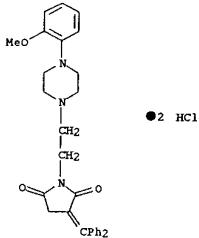
RN 193287-12-6 CAPLUS  
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



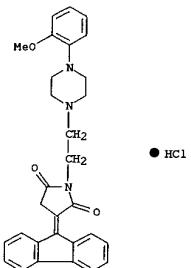
RN 193287-13-7 CAPLUS  
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



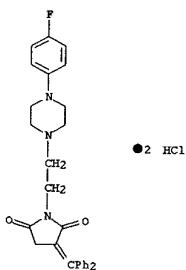
RN 193287-15-9 CAPLUS  
CN 2,5-Pyrrolidinedione,  
3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



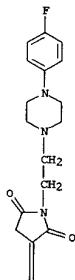
RN 193287-16-0 CAPLUS  
CN 2,5-Pyrrolidinedione,  
3-(diphenylmethylene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



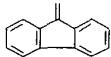
RN 193287-19-3 CAPLUS  
CN 2,5-Pyrrolidinedione,  
3-(9H-fluoren-9-ylidene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 193287-18-2 CAPLUS  
CN 2,5-Pyrrolidinedione,  
3-(9H-fluoren-9-ylidene)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

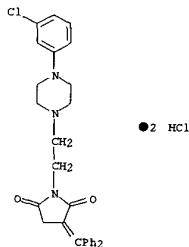


PAGE 2-A



● HCl

RN 220798-76-5 CAPLUS  
 CN 2,5-Pyrrolidinedione,  
 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-  
 (diphenylmethylene)-, dihydrochloride (9CI) (CA INDEX NAME)



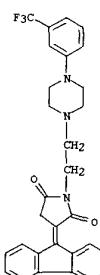
● 2 HCl

RN 220798-85-6 CAPLUS  
 CN 2,5-Pyrrolidinedione,  
 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-(3H-  
 fluoren-9-ylidene)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 220798-90-3 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-(3-  
 (trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, monohydrochloride  
 (9CI) (CA INDEX NAME)

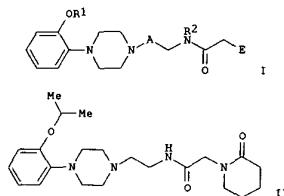


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR  
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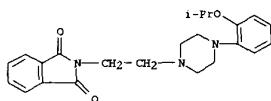
L14 ANSWER 79 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998-764277 CAPLUS  
 DOCUMENT NUMBER: 130:24968  
 TITLE: Preparation of aryl-substituted piperazines useful in the treatment of benign prostatic hyperplasia  
 INVENTOR(S): Jolliffe, Linda; Murray, William; Pulito, Reitz, Alan; Li, Xiaobing; Mulcahy, Linda;  
 Maryanoff, Cynthia; Villani, Frank  
 PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical Inc., USA  
 SOURCE: PCT Int. Appl., 38 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851298	A1	19981119	WO 1998-US9023	19980508
DE, W:	DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, VN, YU, ZW, AM, A2, BY, KG, KZ, MD, RU, TJ, TH, RW: GH, GM, KE, LS, MW, SD, SZ, US, ZW, AT, BE, CH, CT, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9873669	A1	19981208	AU 1998-73669	19980508
EP 984777	A1	20000315	EP 1998-920950	19980508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO				
US 6071915	A	20000606	US 1998-74789	19980508
BR 9809804	A	20000627	BR 1998-9804	19980508
JP 2002511065	T2	20020409	JP 1998-549276	19980508
ZA 9803968	A	19991111	ZA 1998-3968	19980511
NO 9905518	A	20000111	NO 1999-5518	19990111
US 6303594	B1	20011016	US 2000-526224	20000315
PRIORITY APPLN. INFO.: IE, FI, RO				
US 1997-465662	P			
US 1998-74789	A1			
WO 1998-US9023	W			
OTHER SOURCE(S): G1				

MARPAT 130:24968

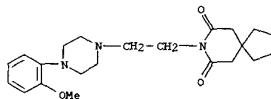


**AB** The title compds. (I; A =  $(CH_2)_n$ ; R1 = H, C1-6 alkyl, (un)substituted Ph, substituted phenyl(C1-5 alkyl); R2 = H, C1-6 alkyl, C1-5 alkenyl, C1-5 alkynyl, (un)substituted phenyl(C1-5 alkyl); E = piperidino, phthalimidio, etc.; n = 1-6) and their pharmaceutically acceptable salts,  $\alpha$ -adrenergic receptor antagonists useful for the therapy of benign prostatic hyperplasia, were prepd. Pharmaceutical compns. contg. I and intermediates used in their manuf. are also claimed. For example, hydrazinolysis of 1-(2-phthalimidinethyl)-4-(2-isopropoxypyhenyl)piperazine with NH<sub>2</sub>OH-HCl gave 1-(2-isopropoxy)-4-(2-isopropoxypyhenyl)piperazine which was amidated with 1-carboxymethyl-2-piperidone (prepn. by N-alkylation of  $\delta$ -valerolactone with BrCH<sub>2</sub>CO<sub>2</sub>Me<sub>3</sub> followed by ester hydrolysis given) to give II. This (as citrate salt) had IC<sub>50</sub> 8.7 nmol for binding on  $\alpha$ .1A receptor subtype cloned with poly(A)+ RNA from human hippocampus and prostate tissue.  
**IT** 216252-67-4  
**RL:** RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and hydrazinolysis; prepn. of aryl-substituted piperazines as  $\alpha$ .1A adrenoceptor antagonists for therapy of benign prostatic hyperplasia)  
**RN** 216252-67-4 CAPLUS  
**CN** 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[2-(1-methylethoxy)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



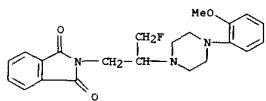
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L14 ANSWER 80 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998-727766 CAPLUS  
 DOCUMENT NUMBER: 130:9074  
**TITLE:**  $\alpha$ .1D-Adrenoceptors contribute to the neurogenic vasopressor response in pithed rats  
**AUTHOR(S):** Rodriguez-Silverio, J.; Castillo, E. F.; Lopez, R. M.; Bobadilla, R. A.; Castillo, C.  
**CORPORATE SOURCE:** Seccion de Estudios de Posgrado e Investigacion, Escuela Superior de Medicina del IPN, Plan de San Luis y Diaz Miron, Casco de Sto Tomas, Mexico, 17, Mex.  
**SOURCE:** Fundamental & Clinical Pharmacology (1998), 12(6), 584-589  
**PUBLISHER:** Editions Scientifiques et Medicales Elsevier  
**DOCUMENT TYPE:** Journal  
**LANGUAGE:** English  
**AB** The aim of the present study was to assess the role of vascular  $\alpha$ .1D-adrenoceptors in the sympathetic vasopressor response in vivo. Specifically, we evaluated the effect of a selective  $\alpha$ .1D-adrenoceptor antagonist, BMY 7378 ( $\beta$ -[3-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl-8-azaspiro(4,5)deca-7,9-dione HCl]) on the vasopressor response induced by preganglionic (T7-T9) sympathetic stimulation in the pithed rat. The vasopressor response was dose-dependently sensitive to inhibition by i.v. BMY 7378 (0.1, 0.31, 1 and 3.1 mg/kg), doses of 1 and 3.1 mg/kg being equally effective. Like BMY 7378, 5-methylurapidil (0.1, 0.31, 1 and 3.1 mg/kg) antagonized the vasopressor response to spinal stimulation; doses of 1 and 3.1 mg/kg were also equally effective. In combination expts., BMY 7378 (1 mg/kg, i.v.) and the  $\alpha$ .1A-adrenoceptor antagonist, 5-methylurapidil (1 mg/kg, i.v.), showed an additive effect. The present results demonstrate that the  $\alpha$ .1D-adrenoceptor subtype plays an important role in the pressor response to sympathetic nerve stimulation in the pithed rat, and confirm the participation of the  $\alpha$ .1A-adrenoceptor subtype in the same response.  
**IT** 21102-95-4, BMY 7378  
**RL:** BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.1D-adrenoceptors contribute to the neurogenic vasopressor response in pithed rats)  
**RN** 21102-95-4 CAPLUS  
**CN** 8-Azaspiro[4.5]decane-7,9-dione, 9-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl  
 REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

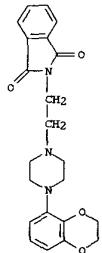
L14 ANSWER 81 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:713719 CAPLUS  
 DOCUMENT NUMBER: 130:52388  
 TITLE: Studies on quinazoline IX. Fluorination versus 1,2-migration in the reaction of 1,3-bifunctionalized amino-2-propanol with DAST  
 AUTHOR(S): Chern, Ji-Wang; Chang, Jun-Yi; Usifoh, Cyril O.; Gutsait, Alexander  
 CORPORATE SOURCE: Sch. Pharmacy, Coll. Medicine, National Taiwan Univ., Taipei, Taiwan  
 SOURCE: Tetrahedron Letters (1998), 39(46), 8483-8486  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 130:52388  
 AB Treatment of 1-phthalylamino-3-[4-(2-methoxyphenyl)piperazin-1-yl]propanol with diethylaminosulfur trifluoride (DAST) induced 1,2-migration via a proposed spiroaziridinium intermediate to give N-[2-fluoro-3-[4-(2-methoxyphenyl)piperazin-1-yl]propyl]phthalimide in 13% yield and N-[2-fluoromethyl-2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]phthalimide in 73% yield.  
 IT 217170-74-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactants or reagent)  
 (fluorination vs. 1,2-migration in reaction of 1,3-bifunctionalized amino-2-propanol with DAST)  
 RN 217170-74-6 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione, 2-[3-fluoro-2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 82 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:660055 CAPLUS  
 DOCUMENT NUMBER: 130:3828  
 TITLE: Functional characteristics of a series of N4-substituted 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazines as 5-HT1A receptor ligands.  
 AUTHOR(S): Van Steen, B. J.; Van Wijngaarden, I.; Ronken, E.; Soudijn, W.  
 CORPORATE SOURCE: Solvay Pharmaceuticals Research Laboratories, Weesp, 1380, Neth.  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(18), 2457-2462  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The agonistic/antagonistic profile of a series of 10 N4-substituted 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazines is evaluated in the *in vitro* adenylyl cyclase assay. The profile is severely affected by the characteristic of the N4-substituents ranging from full agonism (benzamidoethyl deriv.), mixed agonism/antagonism (phthalimidobutyl deriv.) to predominantly antagonism (saccharinbutyl derivative). A novel full antagonist, as potent as WAY 100635, is obtained by substitution of C1 at C-7 of the benzodioxin moiety in the saccharinbutyl derivative.  
 IT 171877-07-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (structure-activity relationship of of (benzodioxinyl)piperazines as 5-HT1A receptor ligands)  
 RN 171877-07-9 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 82 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



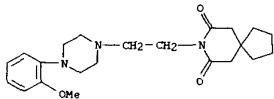
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 83 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:589546 CAPLUS  
 DOCUMENT NUMBER: 129:21129  
 TITLE: .alpha.1L-adrenoceptors in canine pulmonary artery  
 AUTHOR(S): Flavahan, N. A.; Hales, M. A.; Alekowitch, T. D.; Gaine, S. P.; Vanhoutte, P. M.  
 CORPORATE SOURCE: Department of Medicine, Johns Hopkins University, Baltimore, MD, USA  
 SOURCE: Journal of Cardiovascular Pharmacology (1998), 32(2), 308-316  
 PUBLISHER: Lippincott-Raven Publishers  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The aim of this study was to characterize the .alpha.1-adrenoceptors of the canine pulmonary artery. Arterial rings from lower lung lobes were suspended for isometric-tension recording in the presence of cocaine (5 .times. 10<sup>-6</sup> M), hydrocortisone (3 .times. 10<sup>-5</sup> M), propranolol (5 .times. 10<sup>-6</sup> M), and rauwolscine (10<sup>-7</sup> M) to inhibit neuronal uptake, extraneuronal uptake, and .beta.- and .alpha.2-adrenoceptors, resp. Prazosin was more potent against contractions evoked by phenylephrine (pA2 of 9.7) compared with methoxamine (pA2 of 8.4). SZL49 (10<sup>-8</sup> and 3 .times. 10<sup>-8</sup> M), an irreversible .alpha.1-adrenergic antagonist, inhibited responses to phenylephrine but not methoxamine. With norepinephrine, low concns. of prazosin (3 .times. 10<sup>-10</sup> M and 10<sup>-9</sup> M) caused inhibition of the concn.-response curve; a higher concn. (3 .times. 10<sup>-9</sup> M) failed to produce further inhibition, whereas increasing the concn. of the antagonist (to 10<sup>-8</sup> and 3 .times. 10<sup>-8</sup> M) caused further rightward shifts in the concn.-response curve. The Arunlakshana and Schild plot revealed two components corresponding to pA2 values of 9.8 and 8.4. After SZL49 (3 .times. 10<sup>-8</sup> M), the Arunlakshana and Schild plot for the interaction between norepinephrine and prazosin was linear and generated a pA2 of 8.3. Constrictions evoked by phenylephrine were inhibited by the .alpha.1B/.alpha.1D-adrenoceptor antagonist, chloroethylclonidine (10<sup>-5</sup> M), or by the .alpha.1B-antagonist, risperidone (pA2 value of 8.5), but were relatively resistant to inhibition by the selective .alpha.1D-antagonist, BMY7378 (-log KB of 6.1). The results suggest that two .alpha.1-adrenoceptor subtypes mediate contraction of the canine pulmonary artery. One subtype has high affinity for prazosin (.alpha.1H,

L14 ANSWER 83 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 likely to be  $\alpha$ .1B), is activated by phenylephrine, and is inhibited by SZL49. The other subtype has lower affinity for prazosin ( $\alpha$ .1D), is stimulated by methoxamine, and is relatively resistant to SZL49.

The physiol. agonist, norepinephrine, causes contraction by activating both subtypes.

IT 21102-95-4, BMY7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (.alpha.1L-adrenoceptors in canine pulmonary artery)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspido[4.5]decano-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (5Cl) (CA INDEX NAME)



•2 HCl

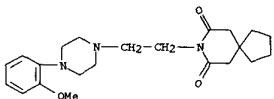
L14 ANSWER 84 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 1998:401962 CAPLUS  
 DOCUMENT NUMBER: 129:130877  
 TITLE: Search for  $\alpha$ .1-adrenoceptor subtypes  
 selective antagonists: design, synthesis and biological activity of cystazosin, an  $\alpha$ .1D-adrenoceptor antagonist  
 AUTHOR(S): Minarini, Anna; Budriesi, Roberta; Chiarini, Alberto  
 CORPORATE SOURCE: Leonardini, Amadeo; Melchiorre, Carlo  
 Department of Pharmaceutical Sciences, University of Bologna, Bologna, I-40126, Italy  
 SOURCE: Biorganic & Medicinal Chemistry Letters (1998), 8(11), 1353-1358  
 PUBLISHER: CODEN: BMCLBZ; ISSN: 0960-894X  
 DOCUMENT TYPE: Elsevier Science Ltd.  
 LANGUAGE: Journal  
 OTHER SOURCE(S): English  
 CASREACT 129:130877  
 AB Two novel quinazolines related to both prazosin and its open analog were synthesized, and their biol. profile at  $\alpha$ .1-adrenoceptor subtypes was assessed by functional assays in rat isolated tissues, namely prostatic vas deferens ( $\alpha$ .1A), spleen ( $\alpha$ .1B) and aorta ( $\alpha$ .1D). Furthermore, the binding profile of cystazosin was assessed at native  $\alpha$ .2A and D2 receptors, and cloned human 5-HT1A receptors, in comparison to prazosin, (+)-cyclazosin, the prazosin open analog and

BMY 7383. It turned out that the cystamine-bearing quinazoline (cystazosin) has a reversed affinity profile relative to (+)-cyclazosin owing to a higher affinity for  $\alpha$ .1B-adrenoceptors and a significantly lower affinity for the  $\alpha$ .1A and  $\alpha$ .1B subtypes. Furthermore, in comparison to BMY 7378, cystazosin displays a much better specificity profile since it has lower affinity for D2 and 5-HT1A receptors.

IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(Search for  $\alpha$ .1-adrenoceptor subtype-selective antagonists by design and synthesis and biol. activity of cystazosin)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspido[4.5]decano-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (5Cl) (CA INDEX NAME)

L14 ANSWER 84 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



•2 HCl

L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 1998:386654 CAPLUS  
 DOCUMENT NUMBER: 129:13120  
 TITLE: Effects of imidazoline derivatives on cholinergic motility in guinea-pig ileum: involvement of presynaptic  $\alpha$ .2-adrenoceptors or imidazoline receptors?  
 AUTHOR(S): Colucci, Roschini; Blandizzi, Corrado; Carignani, Mario; Taccà, Tacca, Department of Oncology, Division of Pharmacology and Chemotherapy, University of Pisa, Via Roma 55, Pisa, I-56126, Italy  
 SOURCE: Naunyn-Schmeidberg's Archives of Pharmacology (1998), 357(6), 682-691  
 PUBLISHER: CODEN: NSAPCC; ISSN: 0028-1298  
 DOCUMENT TYPE: Springer-Verlag Journal  
 LANGUAGE: English  
 AB The present study investigates the possibility that imidazoline receptors mediate modulation of cholinergic motor functions of the guinea-pig ileum. For this purpose, the effects of a series of compds. with known affinity for  $\alpha$ .2-adrenoceptors and/or imidazoline recognition sites were examined. On the radioactivity was taken as an index of endogenous acetylcholine release.  $\alpha$ -Methyl-noradrenaline, noradrenaline, clonidine, mazdacetomidine, oxymetazoline and xylazine caused a concn.-dependent inhibition of twitch responses (IC50 from 0.13 to 1.05  $\mu$ M; Emax from 85.9 to 92.5%). Rilmenidine and agmatine were less potent in reducing the twitch activity, and the latter compd. acted also with low intrinsic activity (IC50=44.9  $\mu$ M; Emax=35.5%). In interaction expts., the inhibitory action of clonidine on twitch responses was competitively antagonized by RX 821002 [2-(2-methoxy-1,4-benzodioxan-2-yl)-2-imidazoline], idazoxan, rauwolscine, yohimbine and BRL 44408

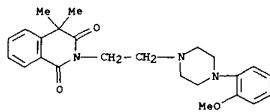
(2-[2H-(1-methyl-1,3-dihydroisoindole)-methyl]-4,5-dihydroimidazoline), whereas prazosin (10  $\mu$ M; BRC 239 [2-(2,4-( $\alpha$ -methoxyphenyl)-piperazin-1-yl)-ethyl]-4,4-dimethyl-1,3-(2H,4H)-isoquinolindione; 10  $\mu$ M) and BRL 41992 [1,2-dimethyl-2,3,9,13b-tetrahydro-1H-dibenzo[*c,f*]imidazol[1,5-*a*]azepine; 10  $\mu$ M] were without effect. Rauwolscine antagonized the

L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
inhibitory effects of various agonists on ileal twitch activity in a competitive manner and with similar potency. Agmatine and idazoxan did not significantly modify the twitch contractions when tested in the presence of .alpha.2-adrenoreceptor blockade by rauwolscine (3 .mu.M) or RX 821002 (1 .mu.M). Linear regression anal. showed that the affinity values of antagonists correlated with their affinity at the .alpha.2A and .alpha.2B binding sites as well as at previously classified .alpha.2A/2B adrenoreceptor subtypes, whereas no significant correlation was obtained when comparing the potency ests. of agonists and antagonists with the affinity at I1 or I2 binding sites. When tested on the elec. induced outflow of tritium, .alpha.-methyl-noradrenaline, noradrenaline, clonidine, medetomidine, oxymetazoline, xylazine and rilmenidine yielded inhibitory concn.-response curves which were shifted rightward to a similar extent in the presence of rauwolscine (3 .mu.M). In the absence of further drugs, agmatine significantly reduced the evoked tritium outflow at the highest concns. tested (10 and 100 .mu.M), whereas idazoxan (up to 100 .mu.M) was without effect. When RX 821002 (1 .mu.M) was added to the superfusion medium, neither agmatine nor idazoxan modified the evoked outflow of radioactivity. The results argue against modulation by imidazoline receptors of acetylcholine release from myenteric plexus nerve terminals. They provide evidence that compds. endowed with imidazoline-like structures affect the cholinergic motor activity of the guinea-pig ileum by interacting with presynaptic .alpha.2-adrenoreceptors belonging to the .alpha.2D subtype.

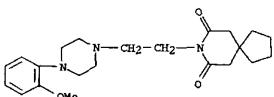
IT 67339-62-2, AR-C 239  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (imidazoline deriv. effect on cholinergic motility in guinea-pig ileum in relation to involvement of presynaptic .alpha.2-adrenoreceptors or imidazoline receptors)

RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-isouquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-dimethyl- (9CI) (CA INDEX NAME)

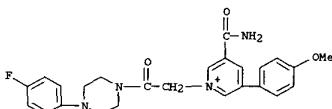
L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 86 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999-340268 CAPLUS  
DOCUMENT NUMBER: 129-62433  
TITLE: Theoretical descriptors in quantitative structure-affinity and selectivity relationship study of potent N4-substituted arylpiperazine 5-HT1A receptor antagonists  
AUTHOR(S): Menziani, M. C.; De Benedetti, P. G.; Karelson, M.  
CORPORATE SOURCE: Dipartimento di Chimica, Universita' di Modena, Modena, 41100, Italy  
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(5), S35-550  
CODEN: RMCECP; ISSN: 0968-0896  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The ability of ad hoc defined size and shape descriptors and theor. descriptors derived on a single structure to give powerful interpretative and predictive QSAR models was compared and evaluated with respect to the quality of the pharmacol. data available for structurally diverse 5-HT1A receptor antagonists, displaying selectivity towards the .alpha.1-adrenergic receptor.  
IT 21102-94-3  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); CAT (Catalyst use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(theor. descriptors in QSAR study of arylpiperazine 5-HT1A receptor antagonists)  
RN 21102-94-3 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



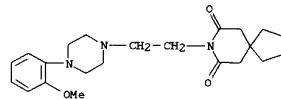
L14 ANSWER 87 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999-340251 CAPLUS  
DOCUMENT NUMBER: 129-81649  
TITLE: Solid phase synthesis of a 1,3,5-trisubstituted pyridinium salt library  
AUTHOR(S): Pradip  
CORPORATE SOURCE: Medicinal Chemistry Department, SmithKline Beecham Pharmaceuticals, Collevalle, PA, 19426-0989, USA  
SOURCE: Tetrahedron Letters (1998), 39(23), 3885-3888  
CODEN: TELEAY; ISSN: 0040-4039  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 129-81649  
AB The synthesis of a 1,3,5-trisubstituted pyridinium salt combinatorial array contg. two variable groups was accomplished in good yields. This entailed the incorporation of 5-bromonicotinic acid onto the resin, followed by Pd(0) catalyzed Suzuki coupling, then alkylation of the pyridine nitrogen and finally cleavage from the resin. A mix and split scheme was also carried out.  
IT 209398-54-9  
RL: SPM (Synthetic preparation); PREP (Preparation)  
(Combinatorial synthesis of a trisubstituted pyridinium salt library)  
RN 209398-54-9 CAPLUS  
CN Pyridinium, 3-(aminocarbonyl)-1-12-[4-(4-fluorophenyl)-1-piperazinyl]-2-oxoethyl-5-(4-methoxyphenyl)-, bromide (9CI) (CA INDEX NAME)



● Br<sup>-</sup>

L14 ANSWER 88 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:319424 CAPLUS  
 DOCUMENT NUMBER: 129:63374  
 TITLE: Pharmacological and immunocytochemical characterization of subtypes of alpha-1 adrenoceptors  
 AUTHOR(S): Low, A. M.; Lu-Chao, H.; Wang, Y. F.; Brown, R.  
 CORPORATE SOURCE: Kwan, C. Y.; Daniel, E. E.  
 SOURCE: Department of Biomedical Sciences, McMaster University, Hamilton, ON, LBN 3Z5, Can.  
 Therapeutics: Journal of Pharmacology and Experimental Therapeutics (1998), 285(2), 694-701  
 PUBLISHER: CODEN: JPETAB; ISSN: 0022-3565  
 WILLIAMS & WILKINS  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In this study, the effects of nine alpha-1 adrenoceptor antagonists [prazosin, WB 4101 (WB), chloroethylclendine (CEC), 5-methylurapidil (5-MU), BMY 7378 (BMY), MDL 73005EF (MDL73), MDL 72832 (MDL72), RS 17053 (RS) and SKF 105854 (SKF)] were studied on contractile responses to phenylephrine (PE) of the endothelium-denuded dog aorta in vitro. All antagonists, except CEC, 5-MU and RS, produced concn.-dependent competitive inhibition of contractile responses of the aorta to PE. The rightward shift of the concn.-response curves of PE yielded const. pKB values with increasing antagonist concns. in most cases allowing a single pooled value to be detd.: for prazosin, a pKB of 8.99+-0.11 (n = 20, KB of 1.03 nM); for WB, a pKB of 8.75+-0.08 (n = 23, KB of 1.76 nM); for BMY, a pKB of 7.21+-0.13 (n = 13, KB of 62 nM); for MDL72, a pKB of 7.95+-0.15 (n = 12, KB of 11.2 nM); and for SKF 105854, a pKB of 5.82+-0.08 (n = 15, KB of 1.52 mu.M). For MDL73, pKB values decreased with antagonist concn.: 7.88+-0.06 at 10 nM, 7.56+-0.28 at 100 nM and 6.92+-0.18 at 1000 nM, which suggests the presence of more than one receptor subtype. CEC (10 and 100 mu.M) almost completely inhibited responses to PE; lower concns. had no significant effect. 5-MU (10-300 nM) and RS (3-300 nM) were ineffective antagonists in this tissue. Because WB, a highly selective alpha-1D and alpha-1A adrenoceptor subtype inhibitor, blocked PE responses (with less affinity than for alpha-1A adrenoceptors), and 5-MU and RS, which are selective blockers for alpha-1A adrenoceptor, were ineffective, we conclude that alpha-1A adrenoceptors are absent in the dog aorta. The effects of the less selective MDL72 were

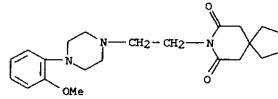
L14 ANSWER 88 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 inconsistent with actions at alpha-1B or alpha-1D adrenoceptors.  
 Although BMY shifted the PE concn.-response curve to the right, the abilities of BMY, MDL73 and SKF to inhibit competitively PE contraction were of lower affinity compared with expectations for interaction with alpha-1D adrenoceptors; they are not the predominant subtype. The complete inhibition of PE responses by CEC suggests that the dog aorta contains the alpha-1B adrenoceptor subtype. In immunocytochem. studies of the expression of alpha-1B adrenoceptor, all cells apparently expressed this protein. Moreover, Western blot studies of the microsomal fractions confirmed the presence of alpha-1B adrenoceptors. In the dog aorta, the alpha-1 adrenoceptors predominantly resemble alpha-1B rather than alpha-1D adrenoceptors as reported in the rat aorta.  
 IT 21102-95-4, BMY 7378  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 alpha-1 adrenoceptors in dog aorta)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

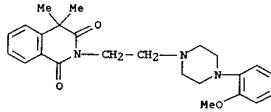
L14 ANSWER 89 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:304032 CAPLUS  
 DOCUMENT NUMBER: 129:62431  
 TITLE: Computer modeling of size and shape descriptors of alpha-1-adrenergic receptor antagonists and quantitative structure-affinity/selectivity relationships  
 AUTHOR(S): Montorsi, Monica; Menziani, M. Cristina; Cocco, Marina; Fanelli, Francesca; De Benedetti, Pier G.  
 CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, Modena, 41100, Italy  
 SOURCE: Methods (Orlando, Florida) (1998), 14(3), 239-254  
 PUBLISHER: CODEN: MTHDE9; ISSN: 1046-2023  
 DOCUMENT TYPE: Academic Press  
 LANGUAGE: English  
 AB Computational chem. and mol. modeling procedures allow the authors to define and compute ad hoc size and shape descriptors on the different prototropic forms assumed by drugs in biotest solns. Together with exptl. data measured on a well-identified target receptor, these descriptors are essential elements for obtaining simple, consistent, comparable, and easily interpretable theor. quant. structure-activity relation (QSAR) models based on the ligand similarity-target receptor complementarity paradigm. In this context, quant. size and shape affinity/subtype selectivity relationships have been modeled for a large set of very heterogeneous .alpha.1a-, .alpha.1b-, and .alpha.1d- adrenergic receptor antagonists. The linear QSAR models generated have been validated by predicting both binding affinity and selectivity of a test set of noncongeneric antagonists. The satisfactory results obtained highlight both the simplicity and the versatility of the approach presented.  
 IT 21102-95-4, BMY 7378 67339-62-2, ARC 239 99718-67-9  
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
 (computer modeling of size and shape descriptors of .alpha.1-adrenergic receptor antagonists and quant. structure-affinity/selectivity relationships)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 89 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

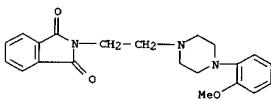


●2 HCl

RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isquinolininedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-dimethyl- (9CI) (CA INDEX NAME)

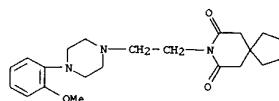


RN 99718-67-9 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 90 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:285099 CAPLUS  
 DOCUMENT NUMBER: 129:63311  
 TITLE: Characterization of .alpha.1-adrenoceptor subtypes in the pig  
 AUTHOR(S): Wikberg-Matsson, Anna; Wikberg, Jarl E. S.; Uhlen, Staffan  
 CORPORATE SOURCE: Academic Hospital, Department of Ophthalmology, Uppsala University, Uppsala, Swed.  
 SOURCE: European Journal of Pharmacology (1998), 347 (2/3), 301-309  
 CODEN: EJPRAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The identities of the .alpha.1-adrenoceptor subtypes present in various tissues of the pig were studied using [<sup>3</sup>H]prazosin radioligand binding. The subtypes were characterized by performing competition expts. for various subtype selective drugs. In the cerebral cortex, spleen and heart, both .alpha.1A- and .alpha.1B-adrenoceptors were detected. In the liver was found only the .alpha.1A-subtype, while in the aorta was found only the .alpha.1B-subtype. An .alpha.1-adrenoceptor subtype was present in the adrenal gland with a high affinity for prazosin, the pKd value being 6.6, but with relatively low affinities for other .alpha.1-adrenoceptor binding drugs. The adrenal gland .alpha.1-adrenoceptor did not seem to represent the classical .alpha.1D-subtype, since drugs selective for the .alpha.1D-subtype in other species, including BMY7378 and SKF104856, showed low affinities for the pig adrenal gland .alpha.1-adrenoceptor.  
 IT 21102-95-4, BMY 7378  
 RL: BPR (Biological process); BSU (Biological study, unclassified);  
 BIOL (Biological study); PROC (Process)  
 (.alpha.1-adrenoceptor subtypes characterization in pig organs)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- dihydrochloride (9CI) (CA INDEX NAME)

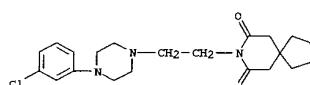
L14 ANSWER 90 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



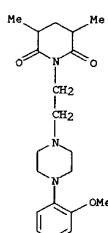
●2 HCl

L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:254237 CAPLUS  
 DOCUMENT NUMBER: 129:22916  
 TITLE: Study of structure-activity relations in a series of buspirone analogs using an electron-topological approach  
 AUTHOR(S): Dimoglo, A. S.; Chumakov, Yu. M.; Simonov, Yu. A.; Andronati, S. A.; Bocelli, G.  
 CORPORATE SOURCE: Inst. Khim., AN Resp. Moldova, Chisinau, Moldova  
 SOURCE: Khimiko-Farmatsevcheskii Zhurnal (1998), 32(1), 36-40  
 CODEN: KHFZAN; ISSN: 0023-1134  
 PUBLISHER: Izdatel'stvo Folium  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB The structure-related psychotropic activity of a series of buspirone analogs is described.  
 IT 21102-97-3 21102-94-3 21103-20-8  
 25024-93-5 25024-94-3 75000-28-1  
 83928-69-2 83928-77-2 83928-78-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (structure-psychotropic activity relations in series of buspirone analogs: electron-topol. approach)  
 RN 21102-97-3 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

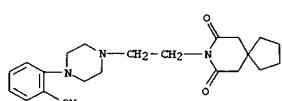
L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 21103-20-8 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

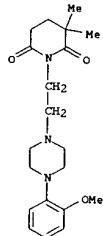


RN 25024-93-5 CAPLUS  
 CN 2,6-Piperidinedione,  
 1-(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-3,5-dimethyl- (9CI) (CA INDEX NAME)

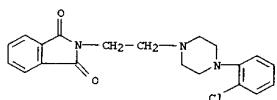


RN 25024-94-6 CAPLUS  
 CN 2,6-Piperidinedione,  
 1-(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-3,3-dimethyl- (9CI) (CA INDEX NAME)

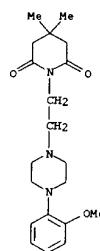




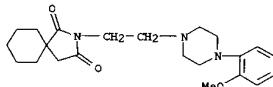
RN 75000-28-1 CAPLUS  
CN 1H-Isoindole-1,3(2H)-dione,  
2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-  
(9CI) (CA INDEX NAME)



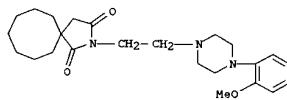
RN 83928-69-2 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,-  
dimethyl- (9CI) (CA INDEX NAME)



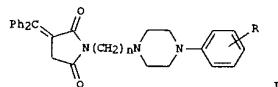
RN 83928-77-2 CAPLUS  
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83928-78-3 CAPLUS  
CN 2-Azaspiro[4.7]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

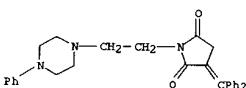


L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1998-220189 CAPLUS  
DOCUMENT NUMBER: 126:308471  
TITLE: 1-[omega-(4-Arylpiperazin-1-yl)alkyl]-3-  
diphenylmethylene-2,5-pyrrolidinediones as 5-HT1A  
receptor ligands: study of the steric  
requirements of the terminal amide fragment on 5-HT1A  
affinity/selectivity  
AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose;  
Rovat,  
Tandu K.; Fernandez, Esther; Sanz, Antonio M.;  
Orensan, Luis  
CORPORATE SOURCE: Departamento de Quimica Organica I, Fac. de  
Ciencias  
SOURCE: Quimicas, Univ. Complutense, Madrid, 28040, Spain  
8(6), 581-586  
PUBLISHER: CODEN: BMCL8; ISSN: 0960-894X  
Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI

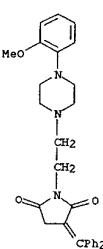


AB Title compds. I [n = 1-4; R = H, 2-OMe, 3-Cl, 4-F] were  
prep'd. from the maleimide, CH2O, and the piperazine or from the maleic anhydride  
and the aminoalkylpiperazine and their binding profiles for the 5-HT1A,  
.alpha.1, and D2 receptors were evaluated. The study of the length  
of the alkyl chain and the imide substructure suggests some important  
differences  
between the non-pharmacophoric sites of both 5-HT1A and  
.alpha.-adrenergic  
receptors, which could be of great importance in designing new  
selective  
ligands.  
IT 206430-38-8P 206430-41-3P 206430-43-5P  
RN 206430-45-7P 206430-46-8P  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
study); PREP (Preparation)  
(steric requirements of the terminal amide fragment of

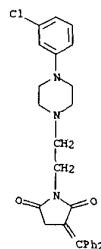
L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
affinity/selectivity)  
RN 206430-38-8 CAPLUS  
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-  
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



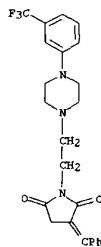
RN 206430-41-3 CAPLUS  
CN 2,5-Pyrrolidinedione,  
3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-  
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



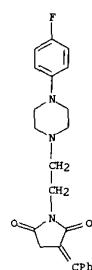
RN 206430-43-5 CAPLUS  
CN 2,5-Pyrrolidinedione, 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-  
(diphenylmethylene)- (9CI) (CA INDEX NAME)



RN 206430-45-7 CAPLUS  
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylen)-1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

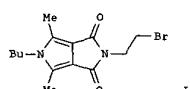
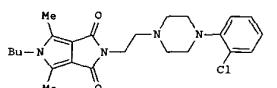


RN 206430-46-8 CAPLUS  
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylen)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

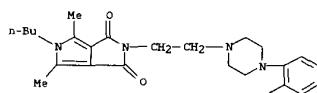


L14 ANSWER 93 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999-261932 CAPLUS  
DOCUMENT NUMBER: 128-78420  
TITLE: Preparation of novel derivative of pyrrole-3,4-dicarboxylic acid imide  
INVENTOR(S): Maria, Wieslaw; Kleinrok, Zdzislaw; Sieklucka,  
Maria  
PATENT ASSIGNEE(S): Akademia Medyczna, Pol.  
SOURCE: Pol., 4 pp.  
CODEN: POXXA7  
DOCUMENT TYPE: Patent  
LANGUAGE: Polish  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 172418	B1	19970930	PL 1993-299531	19930701

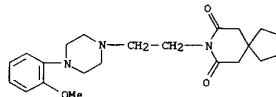


AB The title compd. I, useful as psychotropic, was prep'd. by reacting the imide II with N-(2-chlorophenyl)piperazine in the presence of K<sub>2</sub>CO<sub>3</sub> in MeCN. Compd. I reduced the spontaneous activity in mice at 1/80 LD<sub>50</sub> (LD<sub>50</sub> = 766.3).  
IT 159658-13-6P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prep'n. of novel deriv. of pyrrole-3,4-dicarboxylic acid imide)  
RN 159658-13-6 CAPLUS



L14 ANSWER 94 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:53477 CAPLUS  
 DOCUMENT NUMBER: 128:20086  
 TITLE: Discriminative stimulus effects of 8-hydroxy-2-(di-n-propylamino)tetralin in pigeons and rats: species similarities and differences  
 AUTHOR(S): Klevan, Mark S.; Koek, Wouter  
 CORPORATE SOURCE: Centre de Recherche Pierre Fabre, Castres, 81106, Fr.  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics  
 (1998), 284(1), 238-249  
 PUBLISHER: Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In this study the authors examined the effects of 5-HT1A ligands in rats trained to discriminate 0.16 mg/kg i.p. 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) from saline in a two-key, fixed ratio (FR 10 schedule of food reinforcement, and in pigeons trained to discriminate 0.31 mg/kg i.m. 8-OH-DPAT from saline in a two-key, FR30 schedule of food reinforcement. In both species, 8-OH-DPAT and a variety of structurally unrelated 5-HT1A ligands occasioned dose-related, relatively high levels of drug-appropriate selection (i.e.: *gtreq.678*). A significant pos. correlation was found between estd. ED50 values in both species ( $r = 0.84$ ). Further, 5-HT1A antagonists, NAN-190, penbutolol, (-)-pindolol, tertatolol and WAY-100635, produced dose-related decreases in 8-OH-DPAT-appropriate selection, and their potencies for antagonism in rats and pigeons were highly correlated ( $r = 0.96$ ). The potency of WAY 100635 in rats and pigeons was quantified by Schild anal. (apparent *in vivo* pA<sub>2</sub> values: 7.8 vs. 8.3, rat vs. pigeon, resp.). Although most 5-HT1A agonists produced similar 8-OH-DPAT-like discriminative stimulus effects in both species, two compds., lisuride and eltoprazine, occasioned high levels of drug-appropriate selection in pigeons, but not in rats. In contrast, idazoxan, yohimbine, LER 8804 and BMY 7378 produced greater effects in rats. Among this latter group of compds., only BMY 7378 blocked the discriminative stimulus effects of 8-OH-DPAT in pigeons, which suggested that intermediate levels of drug-appropriate selection obsoled. with the remaining compds. are not necessarily the result of low intrinsic activity. Overall, these results demonstrate similarities in the

L14 ANSWER 94 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 discriminative stimulus effects of 8-OH-DPAT in rats and pigeons despite different training conditions (e.g., training dose and route of administration). Even so, the finding that some 5-HT1A ligands did not produce similar effects in rats and pigeons illustrates the need to examine possible 8-OH-DPAT-like discriminative stimulus effects of compds. in both species.  
 IT 21102-95-4, BMY 7378  
 RL: SAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (discriminative stimulus effects of hydroxy(di-n-propylamino)tetralin in pigeons and rats in relation to species similarities and differences)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



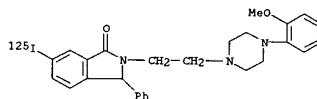
●2 HCl

L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:5220 CAPLUS  
 DOCUMENT NUMBER: 128:110381  
 TITLE: Isoindolin-1-one Analogs of 4-(2'-methoxyphenyl)-1-[2'-(N-(2'-pyridyl)-p-iodobenzamido)ethyl]piperazine [p-MPPI] as 5-HT1A Receptor Ligands  
 AUTHOR(S): Zhuang, Zhi-Ping; Kung, Mei-Ping; Mu, Mu; Kung, Hank F.  
 CORPORATE SOURCE: Departments of Radiology and Pharmacology, University of Pennsylvania, Philadelphia, PA, 19104, USA  
 SOURCE: Journal of Medicinal Chemistry (1998), 41(2), 157-166  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

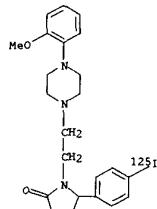
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB In developing radioiodinated antagonists for *in vivo* imaging of 5-HT1A receptors with SPECT, a series of new arylpiperazine benzamido derivs., including I (p-MPPI) ( $K_d = 0.36$  nM), as potential ligands for 5-HT1A receptors were reported previously. However, rapid *in vivo* metab. may have caused the breakdown of the amide bond of [123I]-I and rendered this agent obsolete as an *in vivo* imaging agent in humans. To improve the *in vivo* stability of I, a series of cyclized amide analogs were designed and synthesized. *In vitro* binding, metabolic stability, and *in vivo* biodistribution of these new derivs. were investigated. Several five-membered-ring isoindolin-1-ones displayed very high *in vitro* binding affinity, esp. II ( $R = H$ ,  $R_1 = NO_2$ ;  $R = OH$ ,  $R_1 = iod$ ;  $R = H$ ,  $R_1 = iod$ ), which showed  $K_i$  values of 0.05, 0.65, and 0.07 nM, resp. The affinities for 5-HT1A receptors of other cyclized amide derivs. III ( $R_2 = Br$ ,  $iod$ ) and IV, were 1.09, 2.54, and 14.9 nM, resp. Compared to [125I]-I, iodinated cyclized amide derivs. [125I]-II ( $R = H$ ,  $R_1 = iod$ ) and [125I]-III ( $R_2 = iod$ ) displayed a slower metab. in human liver microsomal and cytosolic prepns. Biodistribution of [125I]-II ( $R = H$ ,  $R_1 = iod$ ) and [125I]-III ( $R_2 = iod$ ) in rats (after an i.v. injection) displayed moderate to low brain uptakes with little or no specific localization in

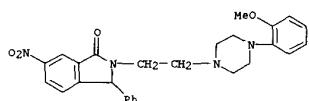
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 hippocampal region, where 5-HT1A receptors are concd. These data indicate that the new iodinated ligands showed high binding affinities and better metabolic stability but displayed unexpectedly low selective binding to 5-HT1A receptors *in vivo*. Addnl. structural modifications may be needed to correct the unfavorable properties displayed for these iodinated cyclized amide derivs. for *in vivo* biodistribution in rats.  
 IT 201531-46-6P 201531-47-7P  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)  
 (prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine isoindolin-1-ones as serotonin 5-HT1A receptor ligands)  
 RN 201531-46-6 CAPLUS  
 CN 1H-Isoindolin-1-one, 2,3-dihydro-6-(iodo-125I)-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



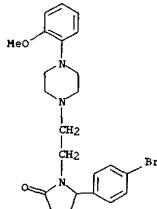
RN 201531-47-7 CAPLUS  
 CN 2-Pyrrolidinone, 5-[4-(iodo-125I)phenyl]-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



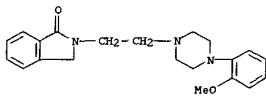
IT 201531-35-3P 201531-36-4P 201531-37-5P  
201531-40-0P 201531-42-2P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); FACT (Reactant or reagent) (prep. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine isoindolone analogs as serotonin 5-HT<sub>1A</sub> receptor ligands)  
RN 201531-35-3 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-nitro-3-phenyl- (9CI) (CA INDEX NAME)



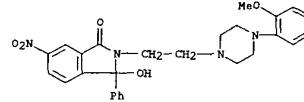
RN 201531-36-4 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-nitro-3-phenyl- (9CI) (CA INDEX NAME)



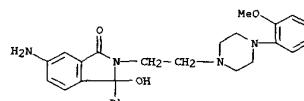
IT 99718-69-1P 201531-33-1P 201531-34-2P  
201531-38-6P 201531-39-7P 201531-41-1P  
201531-44-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prep. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine isoindolone analogs as serotonin 5-HT<sub>1A</sub> receptor ligands)  
RN 99718-69-1 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



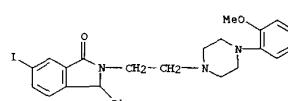
RN 201531-33-1 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



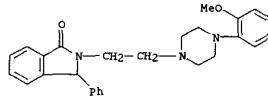
RN 201531-37-5 CAPLUS  
CN 1H-Isoindol-1-one, 6-amino-2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



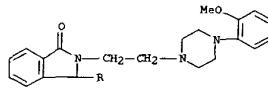
RN 201531-40-0 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-6-iodo-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



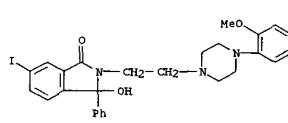
RN 201531-42-2 CAPLUS  
CN 2-Pyrrolidinone, 5-(4-bromophenyl)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



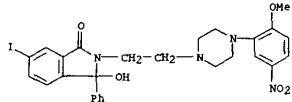
RN 201531-34-2 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-(2-pyridinyl)- (9CI) (CA INDEX NAME)



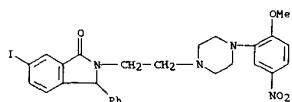
RN 201531-38-6 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-6-iodo-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



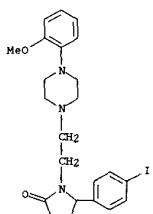
RN 201531-39-7 CAPLUS  
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-6-iodo-2-[2-[4-(2-methoxy-5-nitrophenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 201531-41-1 CAPLUS  
CN 1*H*-isoindol-1-one, 2,3-dihydro-6-iodo-2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

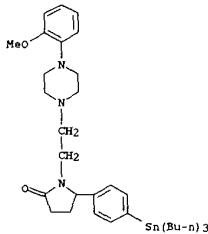


RN 201531-44-4 CAPLUS  
CN 2-Pyrrolidinone, 5-(4-iodophenyl)-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

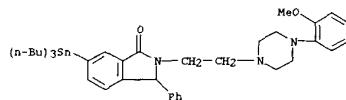


IT 201531-43-3P 201531-45-5P 201532-02-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine

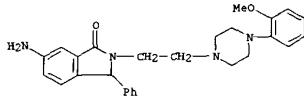
RN 201531-43-3 CAPLUS  
CN 2-pyrrolidinone, 1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-5-[4-(tributylstannylyl)phenyl]- (9CI) (CA INDEX NAME)



RN 201531-45-5 CAPLUS  
CN 1*H*-Isoindol-1-one, 2,3-dihydro-2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-3-phenyl-6-(tributylstannylyl)- (9CI) (CA INDEX NAME)

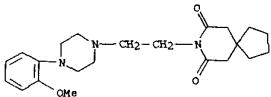


RN 201532-02-7 CAPLUS  
CN 1*H*-Isoindol-1-one, 6-amino-2,3-dihydro-2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



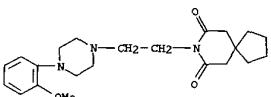
ACCESSION NUMBER: 1998-6089 CAPLUS  
DOCUMENT NUMBER: 128:149828  
TITLE: Pharmacological evidence for  
.alpha.1D-adrenoceptors in the rabbit ventricular myocardium: analysis  
with EMY 7378  
AUTHOR(S): Yang, Tuang-Tian; Endoh, Masao  
CORPORATE SOURCE: Department of Pharmacology, Yamagata University  
School of Medicine, Yamagata, 990-23, Japan  
SOURCE: British Journal of Pharmacology (1997), 122(8), 1541-1550  
CODEN: BJPCBM; ISSN: 0007-1188  
PUBLISHER: Stockton Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB It was examined by means of EMY 7378, a selective antagonist of .alpha.1D-adrenoceptors, whether .alpha.1D-adrenoceptors contribute to the regulation of myocardial contractility and hydrolysis of phosphoinositide in the rabbit ventricular muscle. EMY 7378 had a biphasic antagonistic action on the pos. inotropic effect (PIE) of phenylephrine depending on the concn. EMY 7378 at 1-10 nM shifted the concn.-response curve (CRC) for the PIE of phenylephrine to the right and downward and at 100 nM to 1 .mu.M it antagonized the PIE in a competitive manner, the slope of Schild plot being 0.93 and the pA2 being 7.17.+0.09. The inhibitory action of EMY 7378 at 1-10 nM is ascribed to the selective action on .alpha.1D-adrenoceptors because the PIE of neither isoprenaline nor endothelin-3 and angiotensin II was affected by this compd. over this concn. range. In the presence of 100 nM WB 4101, the antagonistic action of EMY 7378 at 1-10 nM remained unchanged but the antagonistic action of EMY 7378 at 100-300 nM disappeared. The antagonistic action of EMY 7378 at 1 nM was unaffected by 100 nM (+)-niguldipine. Following pretreatment with chloroethylclonidine, EMY 7378 at 1 nM inhibited the maximal response to phenylephrine but the pD2 value for phenylephrine was increased in the presence of EMY 7378. The CRC for phenylephrine was shifted to the left in the presence of 10-100 nM EMY 7378 but it was shifted to the right by EMY 7378 at 300 nM. Stimulation of PI hydrolysis induced by phenylephrine was not affected by EMY 7378 up to 10 nM but it was reduced significantly

L14 ANSWER 96 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 by BMY 7378 at higher concns. (100 nM to 1 μM). BMY 7378 inhibited the [<sup>3</sup>H]prazosin specific binding to the rabbit ventricular membrane fraction in a monophasic manner with a pKi value of 7.53+-0.09. The results indicate that in rabbit ventricular muscle, BMY 7378 at 1-10 nM suppressed the maximal response to phenylephrine (probably mediated by α<sub>1D</sub>-adrenoceptors) and at 10-100 nM it inhibited the neg. inotropic effect of phenylephrine, the mechanisms of which remain to be characterized. At higher concns. (100 nM to 1 μM) BMY 7378 antagonized the functional and biochem. response via a presumed interaction mainly with the α<sub>1B</sub>-adrenoceptor and partially with the α<sub>1A</sub>-adrenoceptor.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 pharmacological evidence for α<sub>1D</sub>-adrenoceptors in rabbit ventricles  
 myocardium using BMY 7378  
 PN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

L14 ANSWER 97 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 indicate that the α<sub>1B</sub> AR mediates the contraction of only the mesenteric resistance artery.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (α<sub>1</sub>-adrenergic receptor subtype localization and contribution to vascular smooth muscle contraction)  
 PN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

L14 ANSWER 97 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:749539 CAPLUS  
 DOCUMENT NUMBER: 128:44122  
 TITLE: Immunocytochemical localization of the α<sub>1B</sub> adrenergic receptor and the contribution of this

and the other subtypes to vascular smooth muscle contraction: analysis with selective ligands and antisense oligonucleotides

AUTHOR(S): Piascik, Michael T.; Hrometz, Sandra L.; Edelmann, Stephanie E.; Guarino, Richard D.J. Hadley, Robert W.,

CORPORATE SOURCE: Brown, R. Dale  
 Department of Pharmacology and Vascular Biology Research Group, University of Kentucky College of Medicine, Lexington, KY, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics

(1997), 283(2), 854-868  
 CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The contribution of the α<sub>1B</sub> adrenergic receptor (AR) to vascular smooth muscle contraction has been assessed using a combination of immunol., mol. biol. and pharmacol. approaches. A subtype-selective antibody detected α<sub>1B</sub> immunoreactivity in the medial layer of the aorta, caudal, femoral, iliac, mesenteric resistance, renal and superior

mesenteric arteries. Receptor protection assays and antisense oligonucleotides were used to assess the contribution of the α<sub>1B</sub>

AR to contraction. The α<sub>1B</sub> AR was implicated in mediating the phenylephrine-induced contraction of the mesenteric resistance artery. The α<sub>1B</sub> AR was implicated in mediating the contraction of the aorta, femoral, iliac and superior mesenteric arteries. Similarly, the α<sub>1B</sub>

AR was implicated in mediating contraction of the caudal and renal arteries. In vivo application of antisense oligonucleotides targeted to

the translational start site of the α<sub>1B</sub> AR had no effect on the phenylephrine-induced contraction of the femoral or renal arteries.

In contrast, antisense oligonucleotides directed against the α<sub>1D</sub> AR significantly inhibited the phenylephrine response in the femoral artery but had no effect on the renal artery. Application of α<sub>1A</sub> AR antisense oligonucleotides inhibited the contraction of the renal artery without effect on the femoral artery. These data show that (1)

α<sub>1B</sub> AR immunoreactivity is widely distributed in the same peripheral arteries

in which previous studies detected its mRNA, and (2) despite this distribution, receptor protection and antisense oligonucleotide studies

L14 ANSWER 98 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:720098 CAPLUS  
 DOCUMENT NUMBER: 128:18934

TITLE: Investigation of α<sub>1</sub>-adrenoceptor subtypes mediating vasoconstriction in rabbit cutaneous resistance arteries

AUTHOR(S): Smith, K. M.; Macmillan, J. B.; McGrath, J. C.  
 Corporate Source: Clinical Research Initiative in Heart Failure, Neuroscience and Biomedical Systems, University of Glasgow, Glasgow, G12 8QQ, UK

SOURCE: British Journal of Pharmacology (1997), 122(5), 825-832

PUBLISHER: Stockton  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Cutaneous resistance arteries (c.r.a.s.) (internal diam.=240.94+-5.42 μm, n=67/25 (no. arteries/no. animals)) from New Zealand white rabbits were mounted in wire myographs and a normalization procedure followed. Cumulative concn.-response curves (CCRCs) were constructed for the α<sub>1</sub>-adrenoceptor agonists noradrenaline (NA), (R)A61603 and phenylephrine (PE) in the presence of cocaine (3 μM), propranolol

(1 μM) and corticosterone (10 μM). The effects of competitive α<sub>1</sub>-adrenoceptor antagonists, prazosin, WB4101, 5-methyl-urapidil, HV723, BMY7378 and the irreversible α<sub>1B</sub> selective compd. chloroethylclonidine (CEC) were examd. vs. the potency and max. response

of the c.r.a.s. to noradrenaline. The high potency of A-61603 relative to PE has been shown to differentiate both functional and binding site α<sub>1A</sub>- or α<sub>1B</sub>-adrenoceptors from α<sub>1D</sub>-adrenoceptors: A-61603 was 944 times more potent than phenylephrine (at EC50)

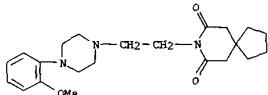
suggesting the presence of a functional α<sub>1A</sub> or α<sub>1B</sub> as opposed to an α<sub>1B</sub> sub-type. Exposure to chloroethylclonidine (CEC, 100 μM) decreased the max. response to noradrenaline but did not significantly change noradrenaline sensitivity indicating that a substantial part of noradrenaline-induced vasoconstriction in rabbit cutaneous arteries is CEC-insensitive. The potencies of prazosin (pA2 = 9.14) and WB4101

(pA2 = 9.30) indicate the involvement of prazosin-sensitive functional α<sub>1</sub>-adrenoceptors. The slopes of corresponding Schild plots for prazosin and WB4101 did not include neg. unity which implies the possible involvement of more than one functional α<sub>1</sub>-adrenoceptor subtype

in noradrenaline-induced vasoconstriction in rabbit cutaneous resistance arteries. In contrast to this, in the case of 5-methyl-urapidil and HV723, the Schild plot slope parameters were not significantly different

from neg. unity over the range of concns. used; the low pA2 value for 5-methylurapidil (7.27) suggests the non-involvement of an α<sub>1A</sub>- or α<sub>1B</sub>-adrenoceptor; the low pA2 value for HV723 (8.47) was similar

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 to that against responses postulated as .alpha.1L. The authors  
 conclude that rabbit cutaneous resistance arteries express a  
 prazosin-sensitive functional .alpha.1-adrenoceptor resembling the .alpha.1B and  
 another low affinity site for prazosin which on the basis of the functional  
 antagonism produced by HV723 most closely resembles the .alpha.1L-adrenoceptor;  
 the low pA<sub>2</sub> value for HV723 (8.47) is similar to that against responses  
 postulated as .alpha.1L.  
 IT 21102-95-4, RMY7378  
 RL RUU (Biological use, unclassified); BIOL (Biological study); USES  
 (Uses)  
 (.alpha.1-adrenoceptor subtypes mediating vasoconstriction in  
 rabbit cutaneous resistance arteries)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-(2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



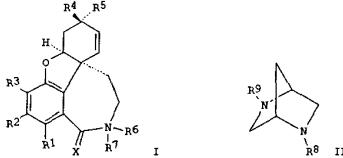
•2 HCl

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 A1 19971030 WO 1997-AT74 19970421  
 DOCUMENT NUMBER: 19971030  
 TITLE: New benzazepine derivatives, medicaments  
 containing the same and their use to prepare medicaments  
 INVENTOR(S): Czollner, Laszlo; Frohlich, Johannes; Jordis, Ulrich;  
 Kuenburg, Bernhard  
 PATENT ASSIGNEE(S): Sanochemia Ltd., Malta; Czollner, Laszlo;  
 Johannes; Jordis, Ulrich; Kuenburg, Bernhard  
 SOURCE: PCT Int. Appl., 136 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740049	A1	19971030	WO 1997-AT74	19970421
DE, LC, PT, VN, GB, GI	DK, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG			
AT 9600716	A	19971015	AT 1996-716	19960419
AT 103003	B	19970525		
AU 9724985	A1	19971112	AU 1997-24985	19970421
EP 897387	A1	19990224	EP 1997-916263	19970421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, FI				
NO 9904852	A	19981116	NO 1998-4852	19981016
PRIORITY APPLN. INFO.: MARPAT 128:13368			AT 1996-716	19960419
GI			WO 1997-AT74	19970421

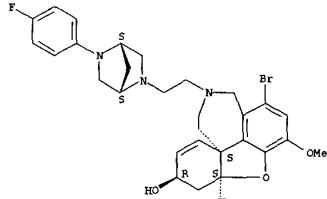
 OTHER SOURCE(S): MARPAT 128:13368

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



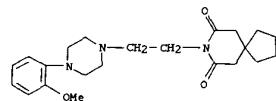
AB The synthesis of benzofuro[3a,3,2,ef][2]benzazepines (I) [R<sub>1</sub>, R<sub>2</sub> = H, halo, CN, NC, OH, SH, SO<sub>2</sub>H, NH<sub>2</sub>, CF<sub>3</sub>, (un)substituted alkyl, (un)substituted aryl, (un)substituted aralkyl, (un)substituted aryloxy; R<sub>3</sub> = OH, OMe; R<sub>4</sub>, R<sub>5</sub> = H, O, substituted O, (un)substituted alkyl, (un)substituted aryl, (un)substituted alkynyl, (un)substituted hydrazine, (un)substituted oxime; X = H<sub>2</sub>, O, and diazabicyclo[2.2.1]heptanes (II) [R<sub>8</sub> = CH<sub>2</sub>Ph, 4-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>, H, (un)substituted alkyl, Me<sub>3</sub>CO<sub>2</sub>C; R<sub>9</sub> = (un)substituted Ph, CH<sub>2</sub>Ph, CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Br, Me<sub>3</sub>CO<sub>2</sub>C] are described. Thus, I (R<sub>1</sub> = Br, R<sub>2</sub> = H, R<sub>3</sub> = OMe, R<sub>4</sub> = OH, R<sub>5</sub> = H, R<sub>6</sub> = H, X = H<sub>2</sub>) (III) was prep'd. by tartrate resoln. of (+)-N-demethyl-8-bromogalanthamine. III in in vitro study showed an IC<sub>50</sub> of >150 n.μmol for the inhibition of acetylcholine esterase. Also disclosed are medicaments which contain compds. of formulas (I) and/or (II) and may be successfully used for treating Alzheimer disease and related dementia states, as well as the Langdon-Down syndrome. IT 199988-64-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepns. of benzazepine galanthamine analogs and diazabicycloheptanes for use in treatment of dementia)  
 RN 199988-64-6 CAPLUS  
 CN 6H-Benzofuro[3a,3,2-ef][2]benzazepin-6-ol, 1-bromo-11-[2-[5-(4-fluorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]ethyl]-4a,5,9,10,11,12-hexahydro-3-methoxy-, [4a.alpha.,6.beta.,8aR\*,11(1R\*,4R\*)]- (9CI) (CA INDEX NAME)

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 Relative stereochemistry.



L14 ANSWER 100 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:713805 CAPLUS  
 DOCUMENT NUMBER: 128:18928  
 TITLE: Antagonism to noradrenaline-induced lethality in rats  
 .alpha.1A-adrenoceptor is related to affinity for the subtype  
 AUTHOR(S): Testa, Rodolfo; Guarneri, Luciano; Iffa, Marina; Angelico, Patrizia; Poggesi, Elena; Teddei, Carlo; Motta, Gianni; Leonardi, Amadeo  
 CORPORATE SOURCE: Pharmaceutical R&D Division, RECORDATI S.p.A., Milan, 20148, Italy  
 SOURCE: Life Sciences (1997), 61(22), 2177-2188 CODEN: LIFSAK; ISSN: 0024-3205  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The potency of several .alpha.1A-adrenoceptor antagonists in preventing the noradrenaline-induced lethality in conscious rats, their binding affinity for the native .alpha.1A- and .alpha.1B-adrenoceptors, the recombinant animal .alpha.1A-, .alpha.1B- and .alpha.1D-adrenoceptor subtypes, as well as their functional affinity for the .alpha.1L-adrenoceptor subtype were evaluated. The potency of the tested compds. as antagonists of noradrenaline-induced lethality was correlated with the affinity for the .alpha.1A- (and .alpha.1A-) adrenoceptor subtype, but not with the affinity for the other subtypes. On the contrary, the hypotensive effects of the compds., assessed in anesthetized rats, were not clearly related with the affinity for any of the .alpha.1-subtypes. These results suggest that the .alpha.1A-subtype plays a detg. role in preventing lethality induced by noradrenaline in the rats, and that this activity is unrelated to the hypotensive effect of the compds., which cannot be clearly correlated with affinity for a particular .alpha.1-adrenoceptor subtype.  
 IT 21102-95-4, EMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);  
 PROC (Process)  
 (antagonism to noradrenaline-induced lethality relation to affinity for .alpha.1A-adrenoceptor subtype)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azazspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (SC1) (CA INDEX NAME)

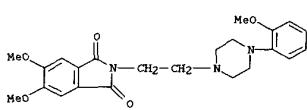
L14 ANSWER 100 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



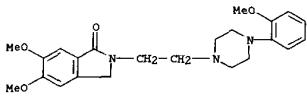
●2 HCl

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:701490 CAPLUS  
 DOCUMENT NUMBER: 128:22921  
 TITLE: Preparation of piperazines having calmodulin inhibitory activity  
 INVENTOR(S): Yamamoto, Kenjiro; Hasegawa, Atsushi; Kubota, Hideki  
 PATENT ASSIGNEE(S): Andodeceased, Masahiro Yamaguchi, Hitoshi Daichi Pharmaceutical Co., Ltd., Japan  
 SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 242,842, abandoned.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 US 5691954 A 19971028 US 1995-416311 19950404  
 PRIORITY APPN. INFO.: JP 1993-11277 19930514  
 US 1994-242842 19940516  
 OTHER SOURCE(S): MARPAT 128:22921  
 GI

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 or in the cerebral region which are caused by excessive activation of calmodulin, were prepnd. Thus, treatment of 1-[(15,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazol-3-yl)acetyl]-4-(3-chloro-2-methylphenyl)piperazine with BH3\*THF in THF afforded the title compd. IV which showed 19.24 increase of survival time on nitrogen-induced hypoxia model in mouse, and IC50 of 3.1 against calmodulin-dependent PDE. IT 198980-97-1P 198981-00-9P 198981-05-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prep. of piperazines having calmodulin inhibitory activity)  
 RN 198980-97-1 CAPLUS  
 CN 1H-Indole-1,3(2H)-dione, 5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (SC1) (CA INDEX NAME)

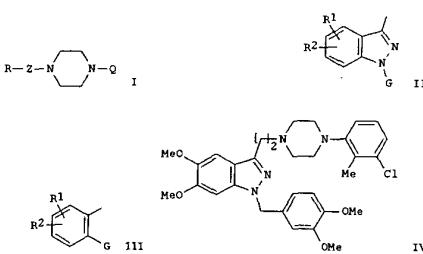


RN 198981-00-9 CAPLUS  
 CN 1H-Indole-1-one, 3-[(3,4-dimethoxyphenyl)methyl]-2,3-dihydro-5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (SC1) (CA INDEX NAME)

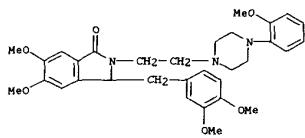


●2 HCl

RN 198981-05-4 CAPLUS  
 CN 1H-Indole-1-one, 3-[(3,4-dimethoxyphenyl)methyl]-2,3-dihydro-5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (SC1) (CA INDEX NAME)



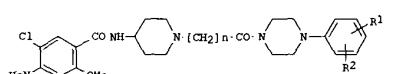
AB The title compds. [I], Q = Cl-6 alkyl, Cl-6 alkoxy, CF<sub>3</sub>, etc.; R = II or III (wherein G = Cl-6 alkyl, (un)substituted Ph, etc.; R<sub>1</sub>, R<sub>2</sub> = Cl-6 alkyl, Cl-6 alkoxy, CF<sub>3</sub>, etc.); Z = Cl-3 alkylene, C<sub>2</sub>-4 alkenylene, C(O), etc., etc., useful as a treating agent for diseases in the circulatory organs



●2 HCl

ACCESSION NUMBER: 1997:618726 CAPLUS  
 DOCUMENT NUMBER: 127:293254  
 TITLE: Preparation of N-(1-substituted-4-piperidyl)benzamides having serotonin receptor agonist activity  
 INVENTOR(S): Yuasa, Teruyuki; Tanaka, Yuji; Khlebnikov, Vladimir  
 Alesevich; Shimamura, Masahiro; Ikeda, Akira; Kobayashi, Hideyuki; Chaki, Etsuko; Takahashi, Kazuyoshi  
 PATENT ASSIGNEE(S): Mitsubishi Chemical Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.  
 CODEN: JKOKAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

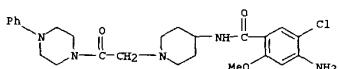
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05241241	A2	19970916	JP 1996-80693	19960308
OTHER SOURCE(S): MARPAT 127:293254				



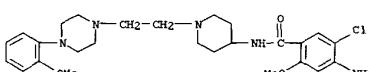
I

AB Title compds. I (R1, R2 = H, halo, lower alkoxy, lower alkyl; X = CO, methylene; n = 1-3) and their pharmaceutically acceptable salts are prepd. 4-Amino-5-chloro-2-methoxy-N-(4-piperidyl)benzamide hydrochloride was treated with 1-(3-chloro-1-oxo-1-propyl)-4-(2-methoxyphenyl)piperazine in HCONMe<sub>2</sub> in the presence of Na<sub>2</sub>CO<sub>3</sub> and NaI at 80.degree. for 4 h to give 97% I (R1 = 2-MeO, R2 = H, X = CO, n = 2) (II), which was treated with oxalic acid in MeOH to give 1.61 g II oxalate. II oxalate showed EC50 of 20.5 nM for relaxation of carbachol-contracted esophageal smooth muscle of rat.  
 IT 197069-60-6P 197069-63-9P 197069-68-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (prepn. of N-(1-substituted-4-piperidyl)benzamides having serotonin agonist activity)

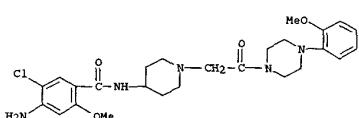
RN 197069-60-6 CAPLUS  
 CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 197069-63-9 CAPLUS  
 CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

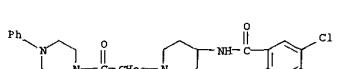


RN 197069-68-4 CAPLUS  
 CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



IT 197069-61-7P 197069-64-0P 197069-69-5P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of N-(1-substituted-4-piperidyl)benzamides having serotonin agonist activity)  
 RN 197069-61-7 CAPLUS  
 CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1  
 CRN 197069-60-6  
 CMF C25 H32 Cl N5 O3



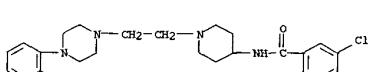
CM 2

CRN 144-62-7  
 CMF C2 H2 O4



RN 197069-64-0 CAPLUS  
 CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1  
 CRN 197069-63-9  
 CMF C26 H36 Cl N5 O3



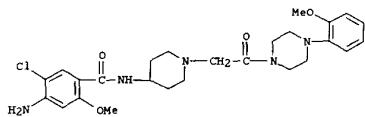
CM 2

CRN 144-62-7  
 CMF C2 H2 O4



BN 197069-69-5 CAPLUS  
 CN Benzanide, 4-amino-5-chloro-2-methoxy-N-[1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)-2-oxoethyl]-4-piperidinyl]-, ethanediatoe (1:1) (9CI)  
 (CA INDEX NAME)

CM 1

CRN 197069-68-4  
 CMF C26 H34 Cl N5 O4

CM 2

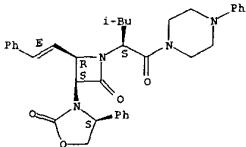
CRN 144-62-7  
 CMF C2 H2 O4

AB Azetidinones I (R1 = H, alkyl, carbamoyl, alkoxy, acyl, benzoyl, phenyl, R2 = H, OH, alkyl; R3 = phthalimido, azido, phenoxycarbamido, oxazolidinone, imidazolinyl, pyrrolidinyl, ureido; Q = O, S, NR5; X = H, alkyl; R5 = H, alkyl, OH, alkoxy, carbonyl, benzyl) were prep'd. for use as vasopressin Vla receptor antagonists. Thus, azetidinone II was prep'd. starting from L-leucine benzyl ester, cinnamaldehyde, and 2-(4(S)-phenyl)oxazolidin-2-one chloride. II gave an IC50 value of 39 nM when tested for vasopressin Vla receptor binding affinity.

IT 195310-53-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prep. of non-peptidyl vasopressin Vla receptor antagonists)

BN 195310-53-3 CAPLUS  
 CN Pipersazine,  
 1-[4-methyl-1-oxo-2-[2-oxo-3-(2-oxo-4-phenyl-3-oxazolidinyl)-4-(2-phenylethynyl)-1-azetidinyl]pentyl]-4-phenyl-, [3S-[1(H+),3.alpha.(R+),4.alpha.(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



ACCESSION NUMBER: 1997-576686 CAPLUS  
 DOCUMENT NUMBER: 127:234215  
 TITLE: Preparation of non-peptidyl vasopressin Vla

INVENTOR(S): Bruns, Robert F., Jr.; Cooper, Robin D. G.; Dressman, Bruce A.; Hundten, David C.; Kaldor, Stephen W.; Koppel, Gary A.; Rizzo, John R.; Skelton, Jeffrey James; et al.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Bruns, Robert F., Jr.; Cooper, Robin D. G.; Dressman, Bruce A.; Hundten, David C.; Kaldor, Stephen W.; Koppel, Gary A.

SOURCE: PCT Int. Appl., 158 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

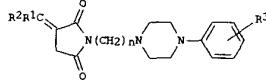
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730707	A1	19970828	WO 1997-US3039	19970220
DE, LC, RO, AM, ML,	DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, X, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, YU, RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, MR, NE, SN, TD, TG			
AU 9719779	A1	19970910	AU 1997-19779	19970220
EP 939632	A1	19990908	EP 1997-907895	19970220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2000504731	T2	20000418	JP 1997-529647	19970220
US 6204260	B1	20010320	US 1999-125737	19990819
US 2002049187	A1	20020425	US 2000-733430	20001208
PRIORITY APPLN. INFO.:			US 1996-12149P	P 19960223
US 1996-12188P			US 1996-12188P	P 19960223
GB 1996-5044			GB 1996-5044	A 19960223
GB 1996-5045			GB 1996-5045	A 19960309
GB 1996-5046			GB 1996-5046	A 19960309
WO 1997-US3039			WO 1997-US3039	W 19970220
US 1999-125737			US 1999-125737	A3 19990819

OTHER SOURCE(S): MARPAT 127:234215  
 GI

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997-549256 CAPLUS  
 DOCUMENT NUMBER: 127-149085  
 TITLE: arylpiperazinylalkylsuccinimides with 5-HT1A and  
 adrenergic.alphal affinity  
 INVENTOR(S): Lopez Rodriguez, Ma. Luz; Morcillo Ortega, Ma.  
 Jose;  
 Rosado  
 K. Rovat, Tandu Fernandez Velando, Esther;  
 Samitier, Ma. Luisa; Oresanz Munoz, Luis Miguel  
 Universidad Complutense De Madrid, Spain  
 SOURCE: Span., 10 pp.  
 CODEN: SPXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Spanish  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2094690	A1	19970116	ES 1994-2396	19941122
ES 2094690	B1	19970801		

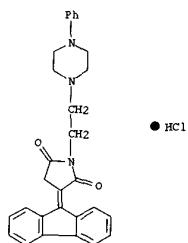
OTHER SOURCE(S): MARPAT 127:149085  
 GI



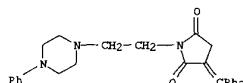
I

AB Title compds. I (R1, R2 = Ph, R1R2 = o-C6H4C6H4-o; R3 = H, alkyl, halogen, alkoxy; n = 1-4) were prep'd. Thus, fluorenone was treated with succinonitrile to give 3-(9H-fluoren-9-ylidene)pyrrolidine-2,5-dione which was treated with 1-(3-trifluoromethylphenyl)piperazine to give I (R1R2 = o-C6H4C6H4-o, R3 = 3-CF3, n = 1, II). II had 5-HT1A affinity of 44.1 nM and .alpha.1 affinity of >1000 nM.  
 IT 193287-12-6P 193287-13-7P 193287-14-8P  
 193287-15-9P 193287-16-0P 193287-17-1P  
 193287-18-2P 193287-19-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); B10L (Biological study); PREP (Preparation); USES (Uses)  
 (prep. of arylpiperazinylalkylsuccinimides with 5-HT1A and adrenergic.alphal affinity)  
 RN 193287-12-6 CAPLUS

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-phenyl)-1-piperazinyl]ethyl-, monohydrochloride (9CI) (CA INDEX NAME)

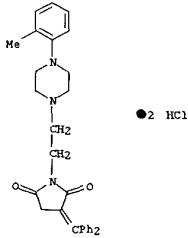


RN 193287-13-7 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

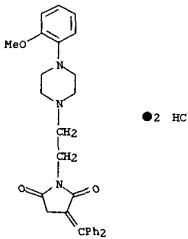


● 2 HCl  
 RN 193287-14-8 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

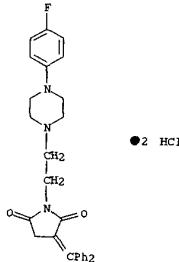


RN 193287-15-9 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

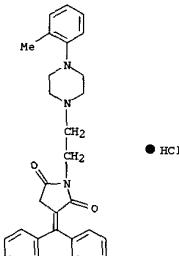


RN 193287-16-0 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-(4-fluorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

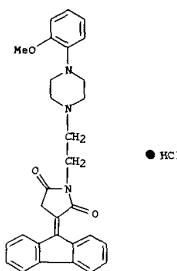
L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 193287-17-1 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

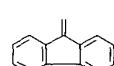
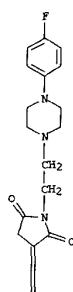


RN 193287-18-2 CAPLUS  
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-(2-methoxyphenyl)-1-



RN 193287-19-3 CAPIUS  
 CN 2,5-Pyrrolidinedione,  
 3-(9H-fluoren-9-ylidene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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● HCl

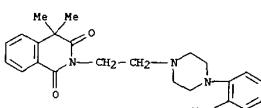
L14 ANSWER 105 OF 263 CAPIUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997-532196 CAPIUS  
 DOCUMENT NUMBER: 127-200050  
 TITLE: Nitrosated and nitrosylated .alpha.-adrenergic receptor antagonist compounds, preparation thereof, compositions containing them, and use in treatment of human impotence or erectile dysfunction  
 INVENTOR(S): Garvey, David S.; Schroeder, Joseph D.; Saenz De Tejada, Inigo  
 PATENT ASSIGNEE(S): Wileman, Inc., USA; Garvey, David S.; Schroeder, Joseph D.; Saenz De Tejada, Inigo  
 SOURCE: PCT Int. Appl., 96 pp.  
 CODEN: PIXMD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9727749	A1	19970807	WO 1997-US1294	19970128
W: AU, CA, IL, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9717562	A1	19970822	AU 1997-17562	19970128
AU 721247	B2	20000629		
JP 2000505424	T2	20000509	JP 1997-537755	19970128
EP 1018879	A1	20000719	EP 1997-904887	19970128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				
PT, SE				
IE, FI				
US 6294517	B1	20010925	US 1998-145143	19980901
US 6323211	B1	20011127	US 1999-285049	19990402
US 6417162	B1	20020709	US 1999-306809	19990507
US 6433182	B1	20020813	US 1999-306805	19990507

PRIORITY APPLN. INFO.: US 1996-595732 A 19960202  
 US 1996-714313 A 19960918  
 WO 1997-US1294 W 19970128  
 US 1998-145143 A2 19980901

OTHER SOURCE(S): MARPAT 127:200050  
 AB Disclosed are nitrosated and nitrosylated .alpha.-adrenergic receptor antagonists, compns. of an .alpha.-adrenergic receptor antagonist optionally substituted with .gtotreq.1 NO or NO<sub>2</sub> moiety, and a compd. that donates, transfers, or releases nitric oxide as a charged species, i.e., nitronium or nitroxyl, or as the neutral species, nitric oxide; and uses for each of them in treating human impotence or erectile dysfunction. Prepn. of compds. of the invention, e.g., N-(N-L-.gamma.-glutamyl-S-nitroso-L-cysteinyl)glycine and 4-[2-(dimethylamino)ethoxy]-2-methyl-5-(1-methylethyl)phenol-(3-S-nitroso-3-methylbutyric acid)ester. The effect of selected compds. on erectile response in rabbits was detd.

L14 ANSWER 105 OF 263 CAPIUS COPYRIGHT 2002 ACS (Continued)  
 IT 67339-62-2, ARC 239  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nitrosated and nitrosylated .alpha.-adrenergic receptor antagonist compds., prepn., compns., adrenergic antagonist-NO donor combinations, and use in treatment of human impotence or erectile dysfunction)  
 RN 67339-62-2 CAPIUS  
 CN 1,3(2H,4H)-Inoquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



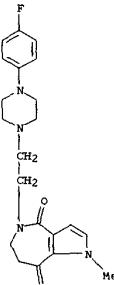
L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:461620 CAPLUS  
 DOCUMENT NUMBER: 127:81465  
 TITLE: Preparation of pyrrolazepine derivatives as serotonin-2 receptor antagonists  
 INVENTOR(S): Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe; Shimamoto, Tetsuo; Nakanishi, Norio  
 PATENT ASSIGNEE(S): Suntory Limited, Japan; Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe; Shimamoto, Tetsuo; Nakanishi, Kyoko; Inomata, Norio  
 SOURCE: PCT Int. Appl., 160 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 970845	A1	19970612	WO 1996-JP3522	19961202
W: AU, CA, HU, IL, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2212092	AA	19970612	CA 1996-2212092	19961202
AU 19967658	A1	19970627	AU 1996-7658	19961202
AU 715220	B2	2000144		
EP 807632	A1	19971119	EP 1996-939340	19961202
EP 807632	BI	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC,				
IE, FI				
IL 121432	A1	20000928	IL 1996-121432	19961202
AT 216388	E	20020515	AT 1996-939340	19961202
US 5962448	A	19991005	US 1997-875495	19970821
US 6258805	BI	20010710	US 1999-312713	19990517
US 2002072515	A1	20020613	US 2002-00021816	20020609
PRIORITY APPLN. INFO.:				
JP 1995-135714	A	19951201		
JP 1996-46928	A	19960209		
WO 1996-JP3522	V	19961202		
US 1997-875495	A2	19970821		
US 1999-312713	A1	19990517		

OTHER SOURCE(S): MARPAT 127:81465  
 GI

L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 and are useful as therapeutic agents for circulatory diseases such as ischemic heart diseases, cerebrovascular disorders, and peripheral circulatory disturbances. Thus, pyrrolazepine deriv. (II) (prepn. given) was reacted with HSCH<sub>2</sub>CH<sub>2</sub>SH in the presence of BF<sub>3</sub>.Et<sub>2</sub>O in AcOH to give 79% the title compd. (III), which at 10<sup>-8</sup> M showed 75.5% inhibitory activity against serotonin (5-HT).  
 IT 191591-85-2P 191592-08-2P  
 RL: BAR (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (propn. of pyrrolazepine derivs. as serotonin-2 receptor antagonists);  
 RN 191591-85-2 CAPLUS  
 CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

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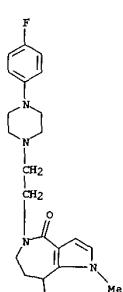
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*  
 AB The title compds. (I) ring F = (un)substituted pyrrole ring; A = alkylene, alkenylene, alkynylene; Y = N-contg. heterocycl, etc; Z1, E2 = H, lower alkyl; dotted line = bond or none) are prepnd. I, having a potent serotonin-2 receptor antagonism, are reduced in toxicity and side effects,

PAGE 2-A

RN 191592-08-2 CAPLUS

L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA INDEX NAME)

L14 ANSWER 107 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:430404 CAPLUS  
 DOCUMENT NUMBER: 127:134218  
 TITLE: In vivo electrophysiological characterization of 5-HT receptors in the guinea pig head of caudate nucleus and orbitofrontal cortex  
 AUTHOR(S): Mansari, M. El; Blier, P.  
 CORPORATE SOURCE: Neurobiological Psychiatry Unit, McGill Univ., Montreal, QC, H3A 1A1, Can.  
 SOURCE: Neuropharmacology (1997), 36(4/5), 577-588  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The aim of the present study was to characterize in vivo the 5-HT receptor subtypes which mediate the effect of microiontophoretic applied 5-HT in the guinea pig head of caudate nucleus and orbitofrontal cortex. 5-HT and the preferential 5-HT<sub>2A</sub> receptor agonist DOI and the preferential 5-HT<sub>2C</sub> receptor agonist mCPP suppressed the quisqualate (QUS)-induced activation of neurons in both structures. The inhibitory effect of DOI and mCPP was not prevented by acute i.v. administration of the 5-HT<sub>1</sub>/receptor antagonist metergoline (2 mg/kg) and the 5-HT<sub>2A/C</sub> receptor antagonist ritanserin (2 mg/kg) in the two regions nor by the selective 5-HT<sub>2A</sub> receptor antagonist MDL100907 (1 mg/kg) in the head of caudate nucleus. However, the inhibitory effect of DOI, but not that of mCPP, was antagonized by a 4-day treatment with metergoline and ritanserin (2 mg/kg/day) using minipumps implanted s.c.) in the head of caudate nucleus, but not in the orbitofrontal cortex. Microiontophoretic ejection of the 5-HT<sub>1A/7</sub> receptor agonist 8-OH-DPAT and of the 5-HT<sub>1A</sub> receptor antagonist WAY100635 both suppressed the spontaneous and QUS-activated firing activity of the orbitofrontal cortex neurons. At currents which did not affect the basal discharge activity of the neuron recorded, microiontophoretic application of WAY100635 and BMY7378 failed to prevent the inhibitory effect of 8-OH-DPAT. The inhibitory effect of gepirone, which is a 5-HT<sub>1A</sub> receptor agonist but devoid of affinity for 5-HT<sub>7</sub> receptors, was also not antagonized by WAY100635. Altogether, these results suggest the presence of atypical 5-HT<sub>1A</sub> receptors in the orbitofrontal cortex. The present results also indicate that the suppressant effect of DOI may be mediated by 5-HT<sub>2A</sub> receptors in the head of caudate nucleus and atypical 5-HT<sub>2</sub> receptors in the orbitofrontal cortex.

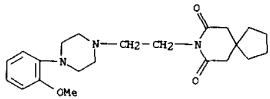


PAGE 1-A

OH

PAGE 2-A

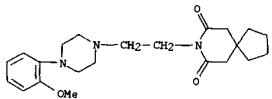
L14 ANSWER 107 OF 263 CAPIUS COPYRIGHT 2002 ACS (Continued)  
 cortex.  
 IT 21102-95-4, BMY7378  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological study, unclassified); BIOL (Biological study)  
 (characterization of 5-HT receptors in guinea pig head of caudate nucleus and orbitofrontal cortex in relation to obsessive compulsive disorder)  
 RN 21102-95-4 CAPIUS  
 CN 8-Azaspiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

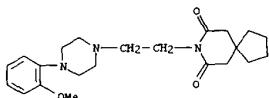
L14 ANSWER 108 OF 263 CAPIUS COPYRIGHT 2002 ACS (Continued)  
 ACCESSION NUMBER: 1997-106096 CAPIUS  
 DOCUMENT NUMBER: 127-130790  
 TITLE: *.alpha.1-Adrenoceptor subtype selectivity: molecular modeling and theoretical quantitative structure-affinity relationships*  
 AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.; Cocchi, M.; Testa, R.; Leonardi, A.  
 CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, Modena, Italy  
 SOURCE: 41100, Italy  
 CODEN: BMECEP; ISSN: 0968-0896  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB This study constitutes a preliminary rationalization, at the mol. level, of antagonist selectivity towards the three cloned .alpha.1-adrenergic receptor (.alpha.1-AR) subtypes. Mol. dynamics simulations allowed a structural/dynamics anal. of the seven .alpha.-helix-bundle models of the bovine .alpha.1a-, hamster .alpha.1b-, and rat .alpha.1d-AR subtypes. The results showed that the transmembrane domains of these subtypes have different dynamic behaviors and different topogs. of the binding sites, which are mainly constituted by conserved residues. In particular, the .alpha.1a-AR binding site is more flexible and topog. different with respect to the other two subtypes. The results of the theor. structural/dynamics anal. of the isolated receptors are consistent with the binding affinities of the 16 antagonists tested towards the three cloned .alpha.1-AR subtypes. Moreover, the theor. quant. structure-affinity relationships obtained from the antagonist-receptor interaction models further corroborate the hypothesis that selectivity towards one preferential subtype is mainly modulated by receptor and/or ligand distortion energies. In other words, subtype selectivity seems to be mainly guided by the dynamic complementarity (induced fit) between ligand and receptor. On the basis of the quant. models presented it is possible to predict both affinities and selectivities of putative .alpha.1-AR ligands, as well as to est. the theor. .alpha.1-AR subtype affinities and selectivities of existing antagonists.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (mol. modeling and QSAR of .alpha.1-Adrenoceptor subtype selectivity)  
 RN 21102-95-4 CAPIUS  
 CN 8-Azaspiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 108 OF 263 CAPIUS COPYRIGHT 2002 ACS (Continued)  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

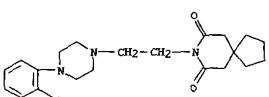
L14 ANSWER 109 OF 263 CAPIUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997-331431 CAPIUS  
 DOCUMENT NUMBER: 127-6047  
 TITLE: *Analysis of .alpha.1-adrenoceptors in rabbit lower urinary tract and mesenteric artery*  
 AUTHOR(S): Duquenne, Chantal; Angel, Itzchak  
 CORPORATE SOURCE: Synthelabo Recherche (L.E.R.S.), Department of Internal Medicine, B.P. 248, 10 rue des Carrières, Rue Malmaison, 92500, Fr.  
 SOURCE: Van der Graaf, Pieter H.; Deplanne, Valerie;  
 25-32 European Journal of Pharmacology (1997), 327(1), CODEN: EJPRAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In this study, we have investigated the effects of a series of .alpha.1-adrenoceptor antagonists on the phenylephrine-mediated contractions of rabbit isolated prostate, urethra, trigone and mesenteric artery. With the exception of RS-17053 (N-[2-(2-cyclopropylmethoxyphenyl)ethyl]-5-chloro-.alpha.,.alpha.-dimethyl-1H-indole-3-ethanamine hydrochloride), the antagonists displayed the lowest potency in the urethra. Catecholamine uptake<sub>1</sub> and uptake<sub>2</sub> appeared not to be the cause for the low pK<sub>B</sub>/pA<sub>2</sub> values obtained in the urethra because cocaine and corticosterone had no effect on the potency of phenylephrine in this tissue. The low potencies displayed by prazosin, RS-17053 and HV723 (.alpha.-ethyl-3,4,5-trimethoxy-.alpha.-(3-((2-(2-methoxyphenyl)ethyl)amino)propyl)benzene-acetonitrile fumarate) suggest that the functional receptors in all four tissues belong to the .alpha.1-adrenoceptor class. Whether or not the significant between-tissue differences in antagonist potencies are due to heterogeneity of this receptor class remains to be elucidated.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (pharmacol. characteristics of the .alpha.1-adrenoceptors in rabbit lower urinary tract and mesenteric artery)  
 RN 21102-95-4 CAPIUS  
 CN 8-Azaspiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-



•2 HCl

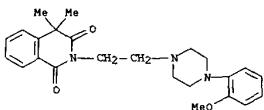
L14 ANSWER 110 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:2294024 CAPLUS  
 DOCUMENT NUMBER: 127:1136  
 TITLE: Is .alpha.1D-adrenoceptor protein detectable in rat tissues?  
 AUTHOR(S): Yang, Ming; Fururth, Frank; Buscher, Rainer;  
 Michel,  
 CORPORATE SOURCE: Martin C.  
 Germany Department Medicine, University Essen, Essen,  
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology  
 (1997),  
 355(4), 438-446  
 CODEN: NSAPCC; ISSN: 0028-1298  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We have used the .alpha.1D-adrenoceptor selective antagonist, BMY 7378, the .alpha.1D-selective agonists, adrenaline and phenylephrine, the .alpha.1A-selective antagonists, (+)-niguldipine, SB 216469 and WB4101, and the non-subtype-selective .alpha.1-adrenoceptor antagonist, nemonapride, to investigate the presence of .alpha.1D-adrenoceptors in rat tissues at the protein level. Radio-ligand binding studies using [<sup>3</sup>H]prazosin as the radio-ligand were performed in three tissues contg. .alpha.1D-adrenoceptor mRNA, spleen, cerebral cortex and kidney, and in comparison in one tissue not contg. .alpha.1D-adrenoceptor mRNA, liver. Cerebral cortex and kidney were also studied upon .alpha.1B-adrenoceptor inactivation by chloroethylclonidine treatment (10 .mu.M, 30 min, 37 degrees). Expts. with cloned rat .alpha.1-adrenoceptor subtypes transiently expressed in COS cells confirmed the known selectivity of the investigated drugs for .alpha.1-adrenoceptor subtypes or the lack thereof of nemonapride. Accordingly nemonapride had steep and monophasic competition curves in all native and chloroethylclonidine-treated tissues. BMY 7378 also had steep and monophasic competition curves and low affinity in all native tissues. In contrast, adrenaline and phenylephrine (in the presence of 100 .mu.M GTP) had monophasic competition curves of low affinity in liver and spleen but biphasic competition curves in cerebral cortex and kidney. Following chloro-ethylclonidine treatment competition curves for adrenaline, phenylephrine, (+)-niguldipine, SB 216469 and WB 4101 remained biphasic in cerebral cortex and kidney while those for nemonapride remained monophasic. We conclude that .alpha.1D-adrenoceptors

L14 ANSWER 110 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 are not readily detectable at the protein level in a variety of rat tissues where their mRNA is expressed. The biphasic competition curves of some agonists and antagonists in chloroethyl-clonidine-treated rat tissues do not represent .alpha.1D-adrenoceptors and are not readily explained by the present .alpha.1A/.alpha.1B/.alpha.1D-adrenoceptor classification.  
 IT 21102-95-4, BMY 7378  
 RL: BPI (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (investigations of presence of .alpha.1D-adrenoceptors in rat tissues at protein level)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

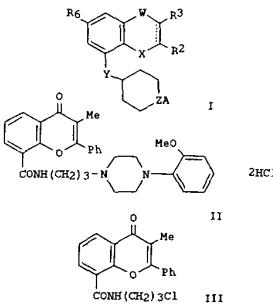
L14 ANSWER 111 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:220142 CAPLUS  
 DOCUMENT NUMBER: 127:176452  
 TITLE: .alpha.2C-adrenoceptors mediate contractile responses to noradrenaline in the human saphenous vein  
 AUTHOR(S): Gavin, K. T.; Colgan, M. P.; Moore, D.; Shanik, G.; Docherty, J. R.  
 CORPORATE SOURCE: Department Physiology, Royal College Surgeons, Dublin,  
 SOURCE: Ire. Naunyn-Schmiedeberg's Archives of Pharmacology  
 (1997), 355(3), 406-411  
 CODEN: NSAPCC; ISSN: 0028-1298  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Postjunctional .alpha.2-adrenoceptors in the saphenous vein were investigated for the ability of .alpha.2-adrenoceptor antagonists to shift the contractile potency of noradrenaline. The following antagonists were employed: chlorpromazine, BDF 8933, prazosin, ARC 239, yohimbine, HV 723, WB 4101, SKF 104078, and BRL 44408. Antagonist potency at postjunctional .alpha.2-adrenoceptors was correlated with antagonist affinity at .alpha.2-adrenoceptor ligand binding sites in membranes of human platelet (.alpha.2), rat kidney (.alpha.2B) and SF 9 cells expressing human recombinant receptors (.alpha.2C). The correlation with the postjunctional .alpha.2-adrenoceptor mediating contraction of the saphenous vein was best for the human recombinant .alpha.2C-adrenoceptor ligand binding site, as compared to correlations with the .alpha.2B-adrenoceptor ligand binding site of rat kidney and with the .alpha.2A-adrenoceptor ligand binding site of human platelet. It is concluded that the functional postjunctional a2-adrenoceptor mediating contractions of the saphenous vein closely resembles the human recombinant a2C-adrenoceptor ligand binding site.  
 IT 67339-62-2, ARC 239  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (affinity of, at the alpha.2-adrenoceptor ligand binding sites in human platelet, rat kidney, human recombinant receptors and potencies in saphenous vein)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolininedione, 2-(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 111 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:169157 CAPLUS  
 DOCUMENT NUMBER: 126:225315  
 TITLE: Bicyclic heterocyclic derivatives having  
 .alpha.1-adrenergic and 5HT1A serotonergic  
 activities  
 INVENTOR(S): Leonardi, Amedeo; Motta, Gianni; Riva, Carlo;  
 Testa,  
 PATENT ASSIGNEE(S): Recordati S.A., Chemical and Pharmaceutical  
 Company,  
 SOURCE: Switz.  
 U.S., 84 pp., Cont.-in-part of U.S. 5,474,994.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

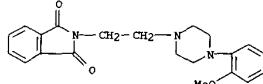
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5605896	A	19970225	US 1994-299188	19940831
US 5403842	A	19950404	US 1992-888775	19920526
AU 9336296	A1	19930913	AU 1993-36296	19930223
RO 111	B1	19930530	RO 1994-1404	19930223
YL 175556	B1	19930913	YL 1994-1089	19930223
RU 2128656	C1	19920410	RU 1994-43324	19930223
SK 280143	B6	19900910	SK 1994-1007	19930223
ZA 9301278	A	19931118	ZA 1993-1278	19930224
LT 3038	B	19940925	LT 1993-354	19930224
CN 1079738	A	19931222	CN 1993-105852	19930526
CN 1040434	A	19981028		
US 5474994	A	19951212	US 1993-67861	19930526
FI 9403876	A	19940823	FI 1994-3876	19940823
NO 9403140	A	19940825	NO 1994-3140	19940825
PRIORITY APPLN. INFO.:				
IT 1992-MI408				
US 1992-299185				
US 1992-67861				
EP 1993-301264				
WO 1993-EF420				

OTHER SOURCE(S): MARPAT 126:225315  
 GI



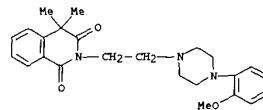
AB Bicyclic heterocyclic derivs., such as I [X = N, O, S; W = C(O), C(S), CH(OH), bond] R2 = H, optionally substituted alkyl, alkenyl, alkynyl, carboxylic acid, heterocycle; R3 = alkyl, hydroxylalkyl, Ph, OH, alkoxy, alkoxylalkyl; R6 = H, halogen, NO2, NH2, AchN, mono-, dialkylamino, CN, CONH, CONH2, CONH, CH(OH), CH:CH, CH:CHCO2, CH:CHCONH, CH2NHCO, CH2NHCO2, CH2O, CH2S, NH, NHCO, NHCONH, NHSO2, O, S, SO2NH, CONHO, CSNH, NHCO2, CO2, CONH(CH2)m, m = 1-6; Z = N, A = (un)substituted Ph, pyrimidinyl, 1,4-benzodioxan-8-yl, benzopyran-8-yl, benzofuran-7-yl, dihydropyran-8-yl; Z = CH2N; Z = CH, A = one or two Ph, 4-FC6H4CO, 2-oxo-1-benzimidazolinyl, (CH2)nON, n = 0-2], and their pharmaceutically acceptable salts useful as .alpha.1-adrenergic and 5HT1A receptor agonists for the treatment of hypertension, urethral and lower urinary tract contractions, and other disorders are described. Thus, benzopyran II was prep'd. by heating 1-(2-methoxyphenyl)piperazine with benzopyran III at 180.degree. for 5 h. II had IC50 = 29 nM for .alpha.1-adrenergic receptor binding, IC50 = 9 nM for 5HT1A receptor binding, ED25 = 45 .mu.g/kg i.v. hypotensive effect and ED25 = 1.4 .mu.g/kg in Na-induced urethral contractility assays.  
 IT 99718-67-9P  
 R1: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)  
 (prepn. of bicyclic heterocyclic derivs. having  
 .alpha.1-adrenergic and  
 5HT1A serotonergic activities)  
 RN 99718-67-9 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione,  
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-  
 (9CI) (CA INDEX NAME)



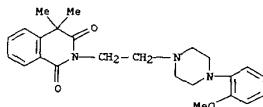
L14 ANSWER 113 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:88411 CAPLUS  
 DOCUMENT NUMBER: 126:113098  
 TITLE: [3H]2-(2-benzofuranyl)-2-imidazoline, a highly selective radioligand for I2-imidazoline receptor binding sites. Studies in rabbit kidney membranes  
 AUTHOR(S): Hosseini, A. R.; King, P. R.; Louis, W. J.; Gundlach, A. L.  
 CORPORATE SOURCE: Austin Repatriation Med. Cent., University Melbourne, Australia  
 SOURCE: Naunyn-Schmiedebergs Archives of Pharmacology (1997), 355 (1), 131-138  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 2-(2-Benzofuranyl)-2-imidazoline (2-BFI) has recently been characterized as a selective ligand for the I2-type of imidazoline-receptor binding site(s) (I2-RBS). The present studies define the relative levels of specific [3H]2-BFI binding to membrane homogenates of brain and kidney from rat, guinea pig and rabbit and identified the pharmacological characteristics of [3H]2-BFI binding sites in rabbit kidney membranes. Rabbit kidney membranes had the highest relative density of specific [3H]2-BFI binding of all tissues studied (2000 fmol/mg protein). Rabbit brain and guinea pig kidney had moderate levels of specific [3H]2-BFI binding (350500 fmol/mg protein), while rat kidney and guinea pig and rat brain displayed much lower densities of binding (4065 fmol/mg protein). Studies of [3H]2-BFI binding kinetics in rabbit kidney homogenates revealed binding to two distinct sites with  $K_d$  values of 0.10 nmol/l and 1.00 nmol/l respectively. Drug inhibition studies revealed that L-adrenalin,  $\alpha$ -adrenoceptor drugs (prazosin, L-phenylephrine) and  $\alpha$ , $\alpha$ -2-adrenoceptor drugs (rauwolscine, methoxydiazokan, ARC-239) had extremely low affinities for [3H]2-BFI binding sites ( $IC_{50}$  > 100 nmol/l). Putative I1-RBS compounds, p-aminoclonidine, moxonidine, imidazole-4-acetic acid and cimetidine, inhibited [3H]2-BFI binding to rabbit renal membranes with low to very low affinities ( $K_i$  values 3 to > 100 nmol/l), suggesting [3H]2-BFI does not label I1-RBS in rabbit kidney membranes. I2-RBS compounds BU224, BU239, idazoxan, and cirazoline inhibited [3H]2-BFI binding confirming the labeling of I2-RBS. Inhibition of [3H]2-BFI binding by certain compounds was consistent with

L14 ANSWER 113 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 their interaction with two binding site populations for example (drug,  $K_i$  values) guanabenz, 0.65 nmol/l and 0.17  $\mu$ mol/l; naphazoline, 0.94 nmol/l and 2.8  $\mu$ mol/l; amiloride, 76 nmol/l and 26  $\mu$ mol/l; rimonidine, 150 nmol/l and 50  $\mu$ mol/l; and clonidine, 230 nmol/l and 70  $\mu$ mol/l. These results demonstrate that [3H]2-BFI is a highly selective and high affinity radioligand for I2-RBS which should be useful for the further characterization of these sites in mammalian tissues.  
 IT 67339-62-2, ARC-239  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (([3H]2-(2-benzofuranyl)-2-imidazoline, a highly selective radioligand for I2-imidazoline receptor binding sites in rabbit kidney and brain)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



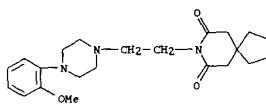
L14 ANSWER 114 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:70989 CAPLUS  
 DOCUMENT NUMBER: 126:113098  
 TITLE: Investigation of the subtype of  $\alpha$ . $\alpha$ .2-adrenoceptor mediating pressor responses in the pithed rat  
 AUTHOR(S): Gavin, Katherine; Docherty, James R.  
 CORPORATE SOURCE: Dep. Physiol., Royal Coll. Surgeons Ireland, Dublin, Ire.  
 SOURCE: European Journal of Pharmacology (1996), 318 (1), 81-87  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We have investigated the subtype of  $\alpha$ . $\alpha$ .2-adrenoceptor mediating postjunctional pressor responses in the pithed rat in comparison with  $\alpha$ . $\alpha$ .2-adrenoceptor ligand binding sites. In pithed rats, postjunctional  $\alpha$ . $\alpha$ .2-adrenoceptors were investigated in terms of the ability of  $\alpha$ . $\alpha$ .2-adrenoceptor antagonists to shift the pressor potency of the  $\alpha$ . $\alpha$ .2-adrenoceptor agonist yohimbine. Antagonist potency at postjunctional  $\alpha$ . $\alpha$ .2-adrenoceptors in the pithed rat was correlated with antagonist affinity at  $\alpha$ . $\alpha$ .2-adrenoceptor ligand binding sites in membranes of rat kidney ( $\alpha$ . $\alpha$ .2B), SF9 cells expressing human recombinant receptors ( $\alpha$ . $\alpha$ .2C) and rat submandibular gland ( $\alpha$ . $\alpha$ .2D) labeled with [ $^3$ H]yohimbine. The correlation with the postjunctional  $\alpha$ . $\alpha$ .2-adrenoceptor mediating pressor responses in the pithed rat was better for the  $\alpha$ . $\alpha$ .2D-adrenoceptor ligand binding site of rat submandibular gland ( $r = 0.95$ ) and the  $\alpha$ . $\alpha$ .2D-adrenoceptor ligand binding site of rat kidney ( $r = 0.90$ ) than with the human recombinant  $\alpha$ . $\alpha$ .2C-adrenoceptor ligand binding site ( $r = 0.81$ ). When the pressor potencies of three additional antagonists were included in the correlations for  $\alpha$ . $\alpha$ .2B- and  $\alpha$ . $\alpha$ .2D-sites only, the correlation with  $\alpha$ . $\alpha$ .2D-adrenoceptor ligand binding site of rat submandibular gland ( $r = 0.91$ ) was much better than with the  $\alpha$ . $\alpha$ .2B-adrenoceptor ligand binding site of rat kidney ( $r = 0.77$ ). It is concluded that the functional postjunctional  $\alpha$ . $\alpha$ .2-adrenoceptors mediating pressor responses in the pithed rat most closely resemble the  $\alpha$ . $\alpha$ .2D-adrenoceptors subtype.  
 IT 67339-62-2, ARC-239  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (subtype of  $\alpha$ . $\alpha$ .2-adrenoceptor mediating pressor responses in pithed

L14 ANSWER 114 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 rat in comparison with ligand binding sites)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 115 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:743484 CAPLUS  
 DOCUMENT NUMBER: 126:152648  
 TITLE: Reduction of guinea pig pup isolation calls by anxiolytic and antidepressant drugs  
 AUTHOR(S): Molewijk, H. E.; Hartog, K.; Van Der Poel, A.  
 M.; Mos,  
 J.; Olivier, B.  
 CORPORATE SOURCE: CNS Pharmacology, Solvay Duphar B. V., Weesp,  
 1380 DA,  
 Neth.  
 SOURCE: Psychopharmacology (Berlin) (1996), 128(1), 31-38  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal Article  
 LANGUAGE: English  
 AB Guinea pigs possess central 5-HT1D receptors similar to humans but different from rats and mice. The effects of a variety of psychotropic drugs on guinea pig pup isolation calls was assessed. Anxiolytic compds. such as the benzodiazepine receptor agonists diazepam and alprazolam, the full 5-HT1A receptor agonists 8-OH-DPAT and flesinoxan, and alc. reduced isolation calling by the guinea pig pup. Moreover, mixed antidepressant/anxiolytic compds. like the 5-HT uptake inhibitors fluvoxamine and clomipramine or the MAO-inhibitor clorgyline as well as the antidepressant NA uptake inhibitors desipramine and maprotiline suppressed vocalizations. The 5-HT1D/1A receptor agonist 5-CT was also very effective in reducing sepn. calls. Remarkably, the partial 5-HT1A receptor agonists buspirone and BMY 7378 did not affect calling. The neuroleptic haloperidol, the psychostimulant d-amphetamine, the putative anxiogenics DMCM and m-CPP and the putative anxiolytics ondansetron and Cl-988 had no effect on isolation calls of guinea pig pups. This paradigm could be helpful to assess behavioral effects of anxiolytic and antidepressant drugs in a species different from rat or mouse, and in which the effects of 5-HT1D receptor ligands may possibly be established.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (redn. of guinea pig pup isolation calls by anxiolytic and antidepressant drugs)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapsiro[4.5]deca-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 115 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

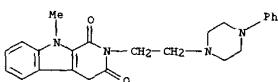


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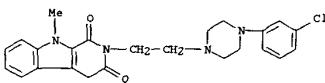
L14 ANSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:731716 CAPLUS  
 DOCUMENT NUMBER: 126:31294  
 TITLE: 4-Aryl-1-piperazinylalkyl derivatives of 1,2,3,4-tetrahydro- $\beta$ -carboline ring system. Synthesis and preliminary in vivo studies  
 AUTHOR(S): Cegla, Marek T.; Boksa, J.; Chojnacka-Wojcik, E.; Misztal, S.  
 CORPORATE SOURCE: Collegium Medicum, Jagiellonian University, Krakow,  
 30688, Pol.  
 SOURCE: Pharmazie (1996), 51(12), 932-936  
 CONP: PHARAT; ISSN: 0031-7144  
 PUBLISHER: Georg Thieme Verlag  
 DOCUMENT TYPE: Journal Article  
 LANGUAGE: English  
 AB Three series of compds. containg a 4-aryl-1-piperazinylalkyl fragment attached to different positions of indole or 1,2,3,4-tetrahydro- $\beta$ -carboline were prep'd. A quant. relationship between the structure of some derivs. and their sedative effect was found using the Free-Wilson approach.  
 IT 184691-40-5P 184691-41-6P 184691-42-8P  
 184691-44-8P 184691-51-8P 184691-52-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FPRP (Synthetic preparation); BIOL (Biological study); FRPR (Preparation) (prepn., sedative effect, antiserotonin activity, and QSAR of (arylpiperazinylalkyl)tetrahydropyridines)  
 RN 184691-40-5 CAPLUS  
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 2-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-, 4,9-dihydro-2-(2-(4-phenyl-1-

L14 ANSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

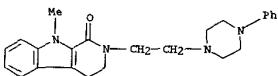
RN 184691-43-8 CAPLUS  
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 4,9-dihydro-9-methyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



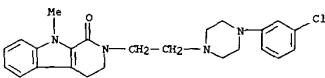
RN 184691-44-9 CAPLUS  
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 2-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-, 4,9-dihydro-9-methyl- (9CI) (CA INDEX NAME)



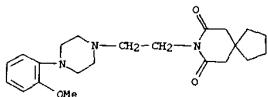
RN 184691-51-8 CAPLUS  
 CN 1H-Pyrido[3,4-b]indol-1-one, 2,3,4,9-tetrahydro-9-methyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 184691-52-9 CAPLUS  
 CN 1H-Pyrido[3,4-b]indol-1-one, 2-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-, 2,3,4,9-tetrahydro-9-methyl- (9CI) (CA INDEX NAME)

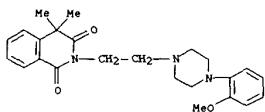


L14 ANSWER 117 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:673359 CAPLUS  
 DOCUMENT NUMBER: 125:31843  
 TITLE: Pharmacological evidence that different .alpha.1 adrenoceptor subtypes mediate contraction in rabbit prostate and hypogastric artery  
 AUTHOR(S): Delafollette, S.; Auguet, M.; Chabrier, P. E.  
 CORPORATE SOURCE: Institut Henri Beaufour Research Labs., Les Ulis, Fr.  
 SOURCE: Acta Physiologica Scandinavica (1996), 158(3), 241-251  
 CODEN: APSCAX; ISSN: 0001-6772  
 PUBLISHER: Blackwell  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The .alpha.1-adrenoceptor subtypes mediating contraction of rabbit prostate and hypogastric artery were pharmacol. characterized using an isolated organ bath technique. The prostate had the same sensitivity to the contractile action of methoxamine and phenylephrine, whereas the hypogastric artery was five times less sensitive to the action of methoxamine in comparison with phenylephrine. Clonidine elicited contraction in the hypogastric artery but not in the prostate.  
 EMY7378  
 Drugs about 70-fold more potent to antagonize the phenylephrine-induced contraction in the hypogastric artery ( $\text{pA}_2$ , 0.14) than in the prostate ( $\text{pA}_2$  6.28), and 5-methyl-urapidil was about three-fold more potent on prostate than on hypogastric artery. The potency of different .alpha.1-adrenoceptor antagonists tested in the rabbit prostate was significantly correlated with their binding affinity for the expressed recombinant .alpha.1A, but no .alpha.1B - or .alpha.1D-, adrenoceptor subtype, whereas, the potency of the .alpha.1-adrenoceptor antagonists tested in the rabbit hypogastric artery was better correlated with the defined .alpha.1D-adrenoceptor. Chlorthalidone produced a 10-fold rightward shift in the phenylephrine conch-response curve in the hypogastric artery but only had a weak effect in the prostate. The results indicates that significant heterogeneity exists among .alpha.1-adrenoceptor in the rabbit hypogastric artery (.alpha.1D-adrenoceptor) and the prostate (.alpha.1A-adrenoceptor).  
 IT 21102-95-4, EMY7378  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 AB Pharmacol. evidence that different .alpha.1 adrenoceptor subtypes mediate contraction in rabbit prostate and hypogastric artery  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]deca-7,9-dione, 9-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



• 2 HCl

L14 ANSWER 118 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:895110 CAPLUS  
 DOCUMENT NUMBER: 125:31851  
 TITLE: The subtype-selective .alpha.2-adrenoceptor antagonists BRL 44408 and ARC 239 also recognize 5-HT1A receptors in the rat brain  
 AUTHOR(S): Meana, J. Javier; Callado, Luis F.; Pazos, Angel; Grijalba, Bernardo; Garcia-Sevilla, Jesus A.  
 CORPORATE SOURCE: Department of Pharmacology, University of the Basque Country, E-48940, Leioa, Spain  
 SOURCE: European Journal of Pharmacology (1996), 312(3), 381-386  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Several .alpha.2-adrenoceptor compds. have been reported to recognize 5-HT1A receptors. The interaction of the .alpha.2A/B- and .alpha.2B/C-adrenoceptor antagonists BRL 44408 (2-[2H-(1-methyl-1,3-dihydroisoindole) methyl]-4,5-dihydroimidazole) and ARC 239 (2-[2-(4-(o-methoxyphenyl)piperazin-1-yl)ethyl]-4,4-dimethyl-1,3-(2H,4H)-isquinolinodine) with 5-HT1A receptors was evaluated in rat brain. Competition assays, the cortex with both compds. against the specific binding of the 5-HT1A receptor radioligand [<sup>3</sup>H]8-OH-DPAT (8-hydroxy-2-(n-propyl)-amino)-tetralin) yielded Ki values in the nanomolar range, fairly close to their previously reported affinities for .alpha.2-adrenoceptors. Similar Ki values were obtained under .alpha.2-adrenoceptor masking conditions by competition assays of these compds. against the .alpha.2-adrenoceptor and 5-HT1A receptor radioligand [<sup>3</sup>H]R 821002 (2-methoxy idazoxan) specific binding in hippocampus. The results indicate that BRL 44408 and ARC 239 recognize 5-HT1A receptors in addn. to .alpha.2-adrenoceptors. The fact should be considered when using these compds. to study .alpha.2-adrenoceptor subtypes.  
 IT 67339-62-2, Arc239  
 RL: BAA (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 ARB 239 recognize 5-HT1A receptors in rat brain  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isquinolinodine, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



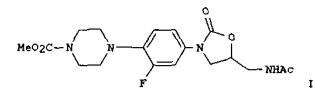
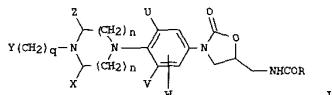
L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:537790 CAPLUS  
 DOCUMENT NUMBER: 125:221870  
 TITLE: (Piperazinylphenyl)oxazolidinone antimicrobials  
 INVENTOR(S): Hutchinson, Douglas K.; Barbachyn, Michael R.;  
 Bricker, Steven J.; Gammill, Ronald B.; Patel,  
 Mahesh

V.  
 PATENT ASSIGNEE(S): Upjohn Co., USA  
 SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 880,  
 432, abandoned.

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5547950	A	19960820	US 1994-332822	19941031
HU 72296	A2	19960429	HU 1994-3208	19930421
CZ 281884	B6	19970312	CZ 1994-2505	19930421
ZA 9302855	A	19941024	ZA 1993-2855	19930422
IL 105555	A1	19980715	IL 1993-105555	19930429
CN 1044236	A	19931229	CN 1993-105039	19930508
CN 1044236	B	19990721		
US 5700799	A	19971223	US 1996-610031	19960304
PRIORITY APPLN. INFO.:			US 1992-880432	B2 19920508
			US 1994-332822	A3 19941031
OTHER SOURCE(S): GI		MARPAT 125:221870		

GI



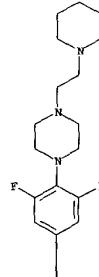
AB Title compds. I or pharmaceutically acceptable salts thereof wherein:  
 each

L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 n is independently 1 to 3; Y is chosen from, e.g., (a) C(O)C1-6 alkyl, C(O)OC1-6 alkyl or benzoyl, (b) N(R3)2 where R3 is independently hydrogen, Cl-4 alkyl or Ph which can be substituted with one to three F, Cl, OH, NH2, or Cl-4 alkyl, wherein each occurrence of said Cl-6 alkyl may be substituted with one or more F, Cl, Br, I, OR1, CO2R1, CN, SR1, or R1 (Where R1 is a hydrogen or Cl-4 alkyl); X and Z are independently C1-6 alkyl, C3-12 cycloalkyl or hydrogen, or X and Z form a C0-3 bridging group, preferably X and Z are hydrogen; U, V and W are independently C1-6 alkyl, F, Cl, Br, hydrogen or a Cl-6 alkyl substituted with one or more of F, Cl, Br or I, preferably U and V are F and W is hydrogen; R is hydrogen, Cl-12 alkyl, C3-12 cycloalkyl, Cl-6 alkoxy, Cl-6 alkyl substituted with one or more F, Cl, Br, I or OH; and q is 0 to 4 inclusive, are useful antimicrobial agents, effective against a no. of human and veterinary pathogens including multiply-resistant staphylococci and streptococci as well as anaerobic organisms such as bacterooides and clostridia species, and acid-fast organisms such as Mycobacterium tuberculosis and Mycobacterium avium. Thus, e.g., arylation of piperazine with 3,4-difluorobromobenzene afforded 1-(2-fluoro-4-nitrophenyl)piperazine; Boc protection followed by redn. provided 1-(tert-butoxycarbonyl)-4-(2-fluoro-4-benzyloxycarbonylamino)laminopiperazine; dihydroxylation followed by cyclization afforded 3-[3-fluoro-4-(4-tert-butoxycarbonylpiperazin-1-yl)phenyl]-5-hydroxymethyl-2-oxazolidinone, the 5-hydroxymethyl group was converted to a 5-acetylaminoethyl group by mesylation, azidification, hydrogenation, and acetylations; finally, Boc deprotection followed by treatment with MeO2CCl afforded oxazolidinone II which exhibited antibacterial activity ED50 of 1.8 mg/kg PO against S. aureus vs. 1.8 mg/kg SC for vancomycin and 2.3 mg/kg PO against S. pyogenes vs. 2.6 mg/kg SC for clindamycin. IT 154590-81-5P 154590-90-6P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) ((piperazinylphenyl)oxazolidinone antimicrobials)  
 RN 154590-81-5 CAPLUS  
 CN Acetamide, N-[(3-[3,5-difluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl)-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.

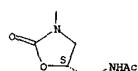
L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 NAME)

Absolute stereochemistry.

PAGE 1-A

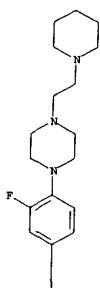


PAGE 2-A



RN 154590-90-6 CAPLUS  
 CN Acetamide, N-[(3-[3-fluoro-4-[4-(2-(1-piperidinyl)ethyl)-1-piperazinyl]phenyl)-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 120 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:435300 CAPLUS  
DOCUMENT NUMBER: 125:104287  
TITLE: Structure activity relationships of a series of buspirone analogs at alpha-1 adrenoceptors:

further evidence that rat aorta alpha-1 adrenoceptors are of the alpha-1D-subtype

AUTHOR(S): Saussy, David L., Jr.; Goetz, Aaron S.; Queen, Thomas

CORPORATE SOURCE: Dep. Receptor Biochem., Glaxo Wellcome, Inc., Research Triangle Park, NC, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics

(1996), 278(1), 136-144 CODEN: JPETAB ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The activity of a series of buspirone analogs at recombinant and rat thoracic aorta alpha-1 adrenoceptors was investigated. Compd.

affinity for recombinant alpha-1A, alpha-1B and alpha-1D adrenoceptors from

human and animal sources was detd. by radioligand binding assays using

membranes prepd. from rat-1 fibroblasts expressing recombinant receptors with

(+)-[125I]iodo-HEAT as the radioligand. Compd. affinity and functional

activity at rat aortic alpha-1 adrenoceptors were detd. using endothelium

denuded rings contracted with phenylephrine. EMY 7378 and MDL 73005EF were found to have significant selectivity for the alpha-1D-subtype

and were high affinity antagonists of the alpha-1 adrenoceptors in the rat aorta. Leverage plot anal. of affinities of the buspirone analogs and a

series of structurally diverse alpha-1 antagonists for recombinant alpha-1

adrenoceptors and rat aorta alpha-1 adrenoceptors demonstrate that the alpha-1 adrenoceptors in the rat aorta are predominantly of the alpha-1D

subtype.

IT 21102-95-4, EMY 7378 25024-76-4 179388-69-3

NAME: BAC (Biological activity or effector, except adverse); BPR

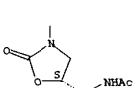
(Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study); PROC (Process); (structure activity relationships of buspirone analogs at

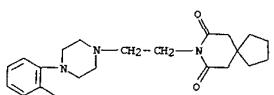
.alpha-1-adrenoceptors and characterization of rat aorta

.alpha-1-adrenoceptors as .alpha.1D subtype)

RN 21102-95-4 CAPLUS

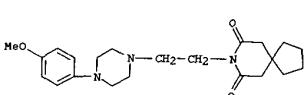


L14 ANSWER 120 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



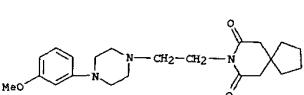
●2 HCl

RN 25024-76-4 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 179388-69-3 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 121 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1996:252231 CAPLUS  
DOCUMENT NUMBER: 124:289578  
TITLE: Preparation of N-[(4-(alkanoyl- and aroyl)piperazinyl)pyridyl]triazolones and analogs

as

INVENTOR(S): Heeres, Jan; Stokbroekx, Raymond Antoine; Mostmans,

PATENT ASSIGNEE(S): Joseph Hector; Van Der Veken, Louis Jozef Elis Janssen Pharmaceutica N.V., Belg.  
SOURCE: PCT Int. Appl., 27 pp.

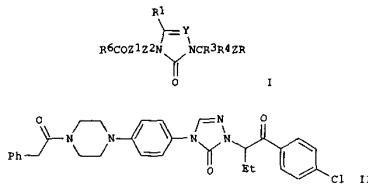
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9601822	A1	19960125	WO 1995-EP2619	19950705
W	AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, LZ, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN			
IT,	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,			
SN, TD, TG				
US 5637592	A	19970610	US 1995-448092	19950523
CA 2193490	AA	19960125	CA 1995-2193490	19950705
AU 9530757	A1	19960209	AU 1995-30757	19950705
AU 685310	B2	19980115		
EP 770074	A1	19970502	EP 1995-926392	19950705
R, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 10171321	A	19970618	CN 1995-194023	19950705
BR 9508377	A	19970529		
HU 76638	A2	19971028	BR 1995-8377	19950705
JP 10502385	T2	19980303	HU 1997-76	19950705
RU 2152392	C1	20000710	JP 1995-504111	19950705
ZA 9505759	A	19970113	RU 1997-102153	19950705
IL 114536	A1	19990411	ZA 1995-7589	19950711
NO 9700088	A	19970310	IL 1995-114536	19950711
FI 9700112	A	19970110	NO 1997-88	19970109
GI			FI 1997-112	19970110
PRIORITY APPLN. INFO.:			EP 1994-202019	A 19940712
OTHER SOURCE(S): MARPAT 124:289578			WO 1995-EP2618	W 19950705



**AB** Title compds. [I; R = (un)substituted Ph; R1-R3 = H, alkyl; R6 = (cyclo)alkyl, (hetero)aryl, etc.; Y = CH or NR; Z = CO, CH(OH); Z1 = piperazine-1,4-di-yl; Z2 = 1,4-phenylene, pyridine-2,5-di-yl, pyrimidine-2,5-di-yl] were prep'd. Thus, title compd. II had MIC of .1toreq.1.mg.M against Helicobacter pylori in vitro.

**IT** 175715-52-3P 175715-53-4P

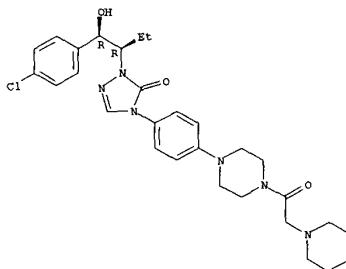
**RL** BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIO (Biological study); PREP (Preparation); USES (Uses) (prepn. of N-[(4-(alkanoyl- and aroyl)piperazino)pyridyl]triazolones and analogs as anti-Helicobacter agents)

**RN** 175715-52-3 CAPLUS

**CN** Piperazine, 1-[4-[1-[4-(4-chlorophenyl)hydroxymethyl]propyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-ylphenyl]-4-(1-piperidinylacetyl)-, (R\*,R\*)- (9CI) (CA INDEX NAME)

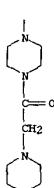
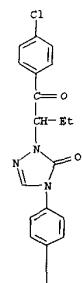
Relative stereochemistry.



**RN** 175715-53-4 CAPLUS

**CN** Piperazine, 1-[4-[1-[1-(4-chlorobenzoyl)propyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-yl]phenyl]-4-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)

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PAGE 2-A

ACCESSION NUMBER: 19961190222 CAPLUS

DOCUMENT NUMBER: 12431306509

TITLE: 2-[4-(6-methoxyphenyl)piperazin-1-ylmethyl]-1,3-disopropoxyimidazo[1,5-a]pyridine as a new selective 5-HT1A receptor ligand

AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose;

Rosado,

M. Luisa Benhamu, Bellinda; Sanz, Antonio M.

CORPORATE SOURCE: Fac. Ciencias Quimicas, Univ. Complutense, Madrid, 28040, Spain

SOURCE: Bioorg. Med. Chem. Lett. (1996), 6(6), 699-94

CODEN: BMCLB, ISSN: 0960-894X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 124:306509

**AB** A series of 2-[4-(*omega*-4-arylpiperazin-1-yl)alkyl]-1,3-

dioxoperyhydroimidazo[1,5-a]pyridine derivs. was prep'd. and evaluated for

affinity at 5-HT1A and  $\alpha$ .<sub>1</sub> receptors. The most promising analog bound at 5-HT1A sites with nanomolar affinity ( $K_i = 31.7$ ) and high selectivity over  $\alpha$ .<sub>1</sub>, D<sub>2</sub> and 5-HT2. $\alpha$ . receptors ( $K_i > 1000$ ,

$K_i > 10\,000$ ,  $K_i > 1000$  nM, resp.). Preliminary studies showed that this agent

is a presynaptic 5-HT1A agonist, and it displayed activity in the face to face behavioral model.

**IT** 21102-94-3

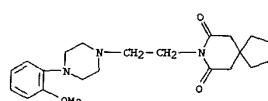
**RL** BPR (Biological process); PRP (Properties); BIOL (Biological study);

PRC (Process) (prepn. of dioxoperyhydroimidazopyridine derivs. as new selective serotoninergic SIA receptor ligands in relation to agonist

activity structure)

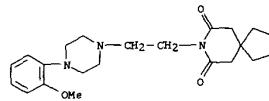
**RN** 21102-94-3 CAPLUS

**CN** 8-azaspiro[4.5]deca-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



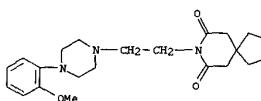
L14 ANSWER 123 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:95589 CAPLUS  
 DOCUMENT NUMBER: 124:232163  
 TITLE: 8-[2-(1,2,3,4-Tetrahydroisoquinolinyl)butyl]-8-azaspiro[4.5]deca-7,9-dione: A New 5-HT1A Receptor Ligand with the Same Activity Profile as Buspirone  
 AUTHOR(S): Mokroso, Jerzy L.; Deren-Wesolek, Anna; Tarczynska, Ewa; Duszynska, Beata; Bojarski, Andrzej J.; Mokroso, Maria J.; Chojnacka-Wojcik, Ewa  
 CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-243, Pol.  
 SOURCE: Journal of Medicinal Chemistry (1996), 39(5), 1125-9  
 CODEN: JMCHAR; ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A new analog of buspirone, i.e., 8-[2-(1,2,3,4-tetrahydroisoquinolinyl)butyl]-8-azaspiro[4.5]deca-7,9-dione (6a), was synthesized. It was demonstrated that buspirone and its analog 6a were equipotent 5-HT1A ligands. Several behavioral models showed that 6a had essentially the same functional profile at 5-HT1A receptors as buspirone. The obtained results permit a conclusion that the basic nitrogen atom and terminal, bulky cycloimide moiety, but not the 2-pyrimidinyl group, of buspirone are directly involved in the formation of the bioactive complex with 5-HT1A receptors.  
 IT 21102-94-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (activity as a 5-HT1A receptor ligand)  
 RN 21102-94-3 CAPLUS  
 CN 6-Azaspiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 123 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 124 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:18915 CAPLUS  
 DOCUMENT NUMBER: 124:46391  
 TITLE: The specific contribution of the novel alpha-1D adrenoceptor to the contraction of vascular smooth muscle  
 AUTHOR(S): Piascik, Michael T.; Guarino, Richard D.; Smith, Marts S.; Soltis, Edward E.; Saussy, David L., Jr.; Perez, Dianne M.  
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Kentucky, Lexington, KY, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1995), 275(3), 1583-8  
 PUBLISHER: Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB With a selective antagonist, the specific contribution of the alpha-1D adrenoceptor (AR) to vascular smooth muscle contraction has been assessed. BMY 7378 bound to membranes expressing the cloned rat alpha-1D AR with a >100-fold higher affinity ( $K_i = 2 \text{ nM}$ ) than binding to either the cloned rat alpha-1A AR ( $K_i = 800 \text{ nM}$ ) or the hamster alpha-1B AR ( $K_i = 600 \text{ nM}$ ). BMY 7378 exhibited differential potency in inhibiting vascular smooth muscle contraction. In the rat aorta and iliac artery, BMY 7378 was a high-affinity antagonist, producing parallel shifts in the phenylephrine concn.-response curve. The dissoon. consts. for this compd. by Schild anal. were 0.95 and 4  $\text{nM}$  for the aorta and iliac artery, resp. The slopes of these Schild plots were not significantly different from unity. BMY 7378 was a weak antagonist in the rat caudal, mesenteric resistance and renal arteries, with Schild slopes significantly <1. With RNase protection assays, alpha-1D mRNA was found in all blood vessels examined. These data suggest that (1) BMY 7378 is a selective alpha-1D AR antagonist that can be used in functional systems to assess the contribution of this receptor in vascular smooth muscle contraction; (2) the alpha-1D AR appears to play a major role in the contraction of the aorta and iliac artery; (3) despite the fact that the mRNA for the alpha-1D AR can be detected in the caudal, mesenteric resistance and renal arteries, it does

L14 ANSWER 124 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 not appear to play a role in mediating contraction of these blood vessels;  
 and (4) expression of alpha-1D mRNA in a particular artery does not ensure that this receptor is involved in regulating the contraction of that artery.  
 IT 21102-95-4, BMY 7378  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (.alpha.1D-adrenoceptor-mediated vascular smooth muscle contraction antagonism by BMY 7378)  
 RN 21102-95-4 CAPLUS  
 CN 6-Azaspiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:916470 CAPLUS  
 DOCUMENT NUMBER: 123:314021  
 TITLE: Preparation of piperazine-substituted pyrroloanthracenes as immunomodulators.  
 INVENTOR(S): Schwerdt, Eckhard; Ladouceur, Gaetan; Kabbe, Hans-Joachim; Aune, Thomas Martin; Bayer A.-G., Germany  
 PATENT ASSIGNEE(S): PCT Int. Appl., 74 pp.  
 SOURCE: CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

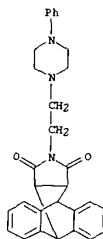
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515946	A1	19950615	WO 1994-EP3934	19941128
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, LK, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, UA, VN MG: RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, EP: BE, CH, DE, FR, GR, IT, LI JP 09506356 T2 19970624				
US 5409932	A	19950425	US 1993-164499	19931209
US 5459143	A	19951017	US 1993-164509	19931209
AU 9512411	A1	19950627	AU 1995-12411	19941128
EP 730040	A1	19950625	EP 1995-903294	19941128
R: CH, DE, FR, GR, IT, LI				
PRIORITY APPN. INFO.:			JP 1994-515534	19941128
			US 1993-164499	19931209
			US 1993-164509	19931209
			WO 1994-EP3934	19941128

OTHER SOURCE(S): MARPAT 123:314021  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

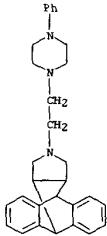
AB Title compds. [I; A, D = H, OH, halo, cyano, CO<sub>2</sub>H, NO<sub>2</sub>, CF<sub>3</sub>, OCF<sub>3</sub>, alkyl, alkoxy; R<sub>1</sub>, R<sub>2</sub> = H, halo, cyano, CHO, Ph, CH, (substituted) alkyl, alkenyl; R<sub>5</sub>, R<sub>6</sub> = H, halo, Ph, (substituted) alkyl; R<sub>7</sub>-R<sub>10</sub> = H, alkyl; R<sub>7</sub>R<sub>8</sub>, R<sub>9</sub>R<sub>10</sub> = O; a = 2-8; R<sub>11</sub> = H, cycloalkyl, pyridyl, pyrimidinyl, (substituted) aryl, alkyl], were prep'd. Thus, 9,10-dihydro-9,10[3',4']-furanocanthracene-12,14(11H,15H)-dione (prepn. given) was refluxed with 3-(4-(4-fluorophenyl)piperazin-1-yl)propylamine (prepn. given) in xylene using a water separator to give 98% title compnd. (II). At 10 mg/kg i.p. in rats, I gave 4-90% inhibition of paw swelling in the adjuvant arthritis

L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 model.  
 IT 169877-38-7P 169877-92-3P  
 RL: BA (Biological activity or effector, except adverse); SPN  
 (Synthesis)  
 preparation; THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)  
 (prep. of piperazine-substituted pyrroloanthracenes as  
 immunomodulators)  
 RN 169877-38-7 CAPLUS  
 CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole,  
 3a,4,9,9a-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



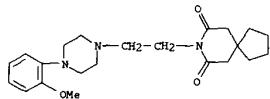
RN 169877-92-3 CAPLUS  
 CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole,  
 2,3,3a,4,9,9a-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



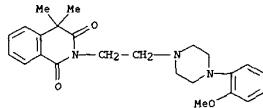
L14 ANSWER 126 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:882567 CAPLUS  
 DOCUMENT NUMBER: 123:314021  
 TITLE: Effects of the NMDA antagonist, dizocilpine, in various drug discriminations: characterization of intermediate levels of drug lever selection  
 AUTHOR(S): Koek, W.; Kleven, M.S.; Colpaert, F.C.  
 CORPORATE SOURCE: Centre de Recherche Pierre Fabre, Castres, 81106, Fr.  
 SOURCE: Behav. Pharmacol. (1995), Volume Date 1995, 6(5 & 6), 590-600  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In each of different groups of rats trained to discriminate either 8-OH-DPAT, DOI, d-amphetamine, cocaine, chlordiazepoxide, or ethanol from saline, dizocilpine produced max. percentages of drug lever (DL) selection that were intermediate between those produced by the training conditions. Dizocilpine also decreased DL selection produced by the training dose in each of the discriminations, except in ethanol-trained rats. In all discriminations, with the exception of ethanol-trained rats, the intermediate levels of DL selection produced by dizocilpine were assoc'd. with increased FRF values (sum of the responses made on either lever before the first reinforcement occurred), increased lever selection latencies, and increased responding on the nonselected lever. At doses that, in general, had effects on response rate similar to those of dizocilpine, intermediate levels of DL selection were produced by WY 7378 in 8-OH-DPAT-trained rats, by WY 50,324 in DOI-trained rats, by (-)-3-PPP in d-amphetamine- and in cocaine-trained rats, by alpidem in chlordiazepoxide-trained rats, and by PCP in ethanol-trained rats. The intermediate levels of DL selection produced by these latter drugs were not assoc'd. with simultaneous increases of FRF values, selection latencies, and responding on the nonselected lever. The results suggest that dizocilpine produces intermediate levels of drug-appropriate responding through the behavioral mechanism of partial generalization only in ethanol-trained rats; in all other discriminations examd. here, the effects of dizocilpine appear to involve (1) pharmacol. effects that differ from those of the training drug, and (2) behavioral mechanisms that are unrelated to stimulus generalization. The differentiation of partial generalization and other mechanisms whereby intermediate responding can occur in the drug discrimination paradigm requires analyses that are more

L14 ANSWER 126 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 detailed than those commonly used in drug discrimination research.  
 IT 21102-95-4, RMY 7378  
 RL: (Biological activity or effector, except adverse); BIOL (Biological study) (effects of the NMDA antagonist, dizocilpine, in various drug discriminations: characterization of intermediate levels of drug lever selection)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decano-7,9-dione, 8-(2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



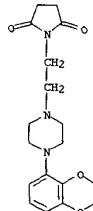
●2 HCl

L14 ANSWER 127 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:828929 CAPLUS  
 DOCUMENT NUMBER: 123:275756  
 TITLE: Identification of drugs subtype-selective for .alpha.2C-adrenoceptors in the pig cerebellum and kidney cortex  
 AUTHOR(S): Wikberg-Matsson, Anna; Wikberg, Jarl E. S.; Uhlen, Staffan  
 CORPORATE SOURCE: Department of Ophthalmology, Academic Hospital, Uppsala, Swed.  
 SOURCE: Eur. J. Pharmacol. (1995), 284(3), 271-9  
 CODEN: EJPHAZ ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB: The radioligands [<sup>3</sup>H]MK512 and [<sup>3</sup>H]RX821002 were used to label .alpha.2A-, .alpha.2B-, and .alpha.2C-adrenoceptors of the pig cerebellum and kidney cortex. By inclusion of the .alpha.2A-adrenoceptor-selective drug, BRL44408, and using a 'multi-curve' exptl. design all the three porcine .alpha.2-adrenoceptor subtypes could be characterized pharmacol. The data indicate that the pig .alpha.2-adrenoceptor subtypes are pharmacol. more related to human .alpha.2-adrenoceptor subtypes than to the rodent .alpha.2-adrenoceptors. The authors suggest a set of drugs that are useful for the delineation of the pig .alpha.2-adrenoceptor subtypes.  
 IT 67339-62-2, AR239  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (identification of drugs subtype-selective for .alpha.2A-, .alpha.2B-, and .alpha.2C-adrenoceptors in the pig cerebellum and kidney cortex)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isodihydroimidinediones, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

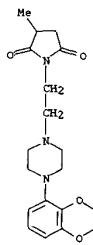


L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:26862 CAPLUS  
 DOCUMENT NUMBER: 124:5550  
 TITLE: A Series of N4-Imidoethyl Derivatives of 1-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazine as 5-HT1A Receptor Ligands: Synthesis and Structure-Affinity Relationships  
 AUTHOR(S): van Steen, B. J.; van Wijngaarden, I.; Tulp, M. Th.  
 M.; Soudijn, W.  
 CORPORATE SOURCE: Department of Medicinal Chemistry, Solvay Duphar Research Laboratories, Weesp, 1380 DA, Neth.  
 SOURCE: Journal of Medicinal Chemistry (1995), 38(21), 4303-8  
 CODEN: JMCMAR ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB: A series of unsubstituted and substituted succinimido, maleimido, and glutarimidoethyl derivs. of eltoprazine was synthesized and tested for affinity for the 5-HT1A receptor in rat brain homogenates. The unsubstituted compds. have a moderate affinity for the receptor, while the affinity considerably increases by substitution at or enlargement of these cyclic ring systems. A good correlation was found between the inhibition const. Ki (expressed as pKi) and the lipophilicity (clogP). No correlation was obsd. between the pKi or pKi<sup>+</sup> (local inhibition const.) and the basicity of the N4-nitrogen atom.  
 IT 171877-00-2P 171877-7-3P 171877-02-4P 171877-03-5P 171877-08-5P 171877-09-6P 171877-10-4P 171877-11-5P 171877-13-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis and structure-affinity relationships of N4-imidoethyl derivs. of (Dihydrobenzodioxinyl)piperazine)  
 RN 171877-00-2 CAPLUS  
 CN 2,5-Pyrrolidinediones, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

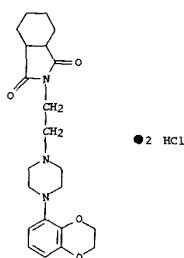
L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



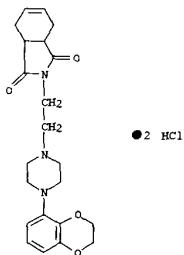
RN 171877-01-3 CAPLUS  
 CN 2,5-Pyrrolidinediones, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-3-methyl- (9CI) (CA INDEX NAME)



RN 171877-02-4 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione, 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]hexahydro-, dihydrochloride (9CI) (CA INDEX NAME)



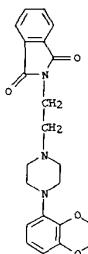
RN 171877-03-5 CAPLUS  
CN 1H-Isindole-1,3(2H)-dione,  
2-[2-(4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl)ethyl]-3a,4,7,7a-tetrahydro-, dihydrochloride (9CI) (CA INDEX NAME)



RN 171877-08-0 CAPLUS  
CN 1H-Isindole-1,3(2H)-dione,  
2-[2-(4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-

piperazinyl)ethyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

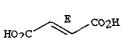
CM 1

CRN 171877-07-9  
CMF C22 H23 N3 O4

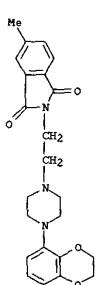
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

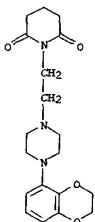
Double bond geometry as shown.



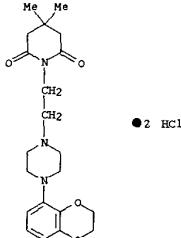
RN 171877-09-1 CAPLUS  
CN 1H-Isindole-1,3(2H)-dione,  
2-[2-(4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl)ethyl]-5-methyl- (9CI) (CA INDEX NAME)



RN 171877-10-4 CAPLUS  
CN 2,6-Piperidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

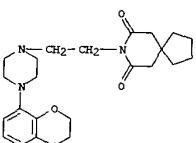


RN 171877-11-5 CAPLUS  
CN 2,6-Piperidinedione, 1-(2-(4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl)ethyl)-4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



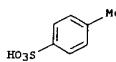
RN 171877-13-7 CAPLUS  
CN 8-(4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl)ethyl-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

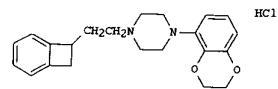
CRN 171877-12-6  
CMF C23 H31 N3 O4

CM 2

CRN 104-15-4  
CMF C7 H8 O3 S



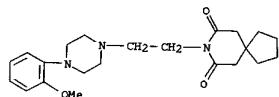
L14 ANSWER 129 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:790900 CAPLUS  
 DOCUMENT NUMBER: 124:134742  
 TITLE: Characterization of Potent and Selective  
 Antagonists  
 at Postsynaptic 5-HT1A Receptors in a Series of  
 N4-Substituted Arylpiperazines  
 AUTHOR(S): Peglion, Jean-Louis; Canton, Herve; Bervoets,  
 Karin;  
 Alain;  
 CORPORATE SOURCE: Le Marquille-Girardon, Sylvie; Millan, Mark J.  
 Fr.;  
 SOURCE: Institut de Recherches Servier, Suresnes, 92150,  
 4044-55  
 PUBLISHER: Journal of Medicinal Chemistry (1995), 38(20),  
 DOCUMENT TYPE: CODEN: JMCMAR; ISSN: 0022-2623  
 LANGUAGE: American Chemical Society  
 English  
 G1



AB Benzocycloalkyl and benzocycloalkenyl moieties linked, directly or via an alkyl chain, to oxygen-bearing heteroarylpirperazines were synthesized, in an attempt to obtain potent and selective antagonists at postsynaptic 5-HT1A receptors. From the numerous arylpiperazines described in the literature, 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazine was chosen as a model of an arylpiperazine in view of its selectivity for 5-HT1A receptors vs. .alpha.1-, .alpha.2-, and .beta.-adrenergic receptors, as well as dopamine D1 and D2 receptors. Two other closely-related arylpiperazines, 1-(1,5-benzodioxepin-6-yl)piperazine and 1-(benzofuran-7-yl)piperazine, were also examed, in this study. All compds. showed high affinity at 5-HT1A sites ( $K_{i}$  = 9.10 nM,  $K_{D}$  = 9.35), and the majority behaved as antagonists *in vivo* in blocking the hypothermia induced by the 5-HT1A agonist 8-OH-DPAT in the absence of a marked effect alone at equiv. doses. An *in vivo* evaluation of dopamine D2 receptor antagonist properties revealed that the majority of compds. was devoid of activity at this site,

L14 ANSWER 129 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 in marked contrast to BMY 7378 which displayed virtually no selectivity for 5-HT1A vs. dopamine D2 receptors. Moreover, six compds. of the present series, including I, showed >10-fold selectivity *in vitro* over 5-HT1A vs. .alpha.1-adrenergic receptors. I displayed an optimal compromise between potency ( $pK_i$  = 8.75), marked antagonist activity, and selectivity toward .alpha.1-adrenergic (81-fold) and dopamine D2 receptors. These characteristics clearly distinguish I from previously-reported ligands such as the postsynaptic 5-HT1A antagonist BMY 7378 and the weak partial agonist NAN 190 which, in contrast to the compds. of this series, belong to the well-exemplified class of imido derivs. of (o-methoxyphenyl)piperazines. The availability of I (S 15535) should facilitate the further elucidation of the functional role and potential therapeutic significance of 5-HT1A receptors.

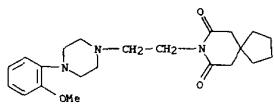
IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BUU (Biological study, unclassified); BIOL (Biological study) (potent and selective antagonists at postsynaptic 5-HT1A receptors in a series of N4-substituted arylpiperazines)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 130 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:698387 CAPLUS  
 DOCUMENT NUMBER: 123:103264  
 TITLE: Studies on the role of 5-HT1A autoreceptors and .alpha.1-adrenoceptors in the inhibition of 5-HT release. I. BMY7378 and prazosin  
 AUTHOR(S): Björk, S.; Bengtsson, H. J.; Milano, S.; Lundberg, J.; Sharp, T.  
 CORPORATE SOURCE: Dep. Pharmacology, Univ. Göteborg, Göteborg, Sweden.  
 SOURCE: Neuropharmacology (1995), 34(6), 615-20  
 DOCUMENT TYPE: CODEN: NEPHBW; ISSN: 0028-3908  
 LANGUAGE: Journal English  
 AB The present study utilized *in vivo* microdialysis to investigate the importance of 5-HT1A autoreceptors and .alpha.1-adrenoceptors in the decreased 5-HT release obtained following administration of the mixed 5-HT1A autoreceptor/partial agonist/.alpha.1-adrenoceptor antagonist BMY 7378, the selective 5-HT1A receptor agonist 8-OH-DPAT and the .alpha.1-adrenoceptor antagonist prazosin. BMY 7378 (0.25 mg/kg, s.c.), 8-OH-DPAT (0.025 mg/kg, s.c.) and prazosin (0.1-1.0 mg/kg, s.c.) all suppressed ventral hippocampal 5-HT efflux. The BMY 7378 and 8-OH-DPAT-induced inhibition of 5-HT release were reversed by a 40 min pretreatment with either (+/-)pindolol (8 mg/kg, s.c.) or WAY-100635 (0.3 mg/kg, s.c.), to block 5-HT1A autoreceptors. Neither of these antagonists altered the prazosin-induced (0.3 mg/kg, s.c.) 5-HT decrease. The results: (i) confirm that both an .alpha.1-adrenoceptor antagonist (prazosin) and 5-HT1A autoreceptor stimulants (BMY 7378 and 8-OH-DPAT) may reduce cerebral 5-HT release; (ii) support that the BMY 7378-induced decrease in 5-HT release results from 5-HT1A autoreceptor agonism, rather than .alpha.1-adrenoceptor blockade; and (iii) argue against "physiol." antagonism (i.e. via blockade of .beta.-adrenoceptors, 5-HT1B receptors or some other mechanism) as an explanation for the reversal by pindolol of 5-HT1A autoreceptor agonist-induced suppression of 5-HT release. These data support the usefulness of pindolol, as well as the more specific compd. WAY-100635, to block 5-HT1A autoreceptors.

IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (5-HT1A autoreceptors and .alpha.1-adrenoceptors in inhibition of hippocampal 5-HT release)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

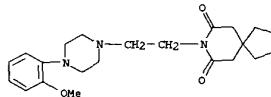


●2 HCl

L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995-644351 CAPLUS  
 DOCUMENT NUMBER: 123:26183  
 TITLE: Modulation of the activity of central serotonergic neurons by novel serotonin1A receptor agonists and antagonists: a comparison to adrenergic and dopaminergic neurons in rats  
 AUTHOR(S): Gobert, A.; Lejeune, F.; Rivet, J.-M.; Audinot, Newman-Tancredi, A.; Millan, M. J.  
 CORPORATE SOURCE: Dep. of Psychopharmacology, Inst. Recherches Servier, Croissy-sur-Seine, 78290, Fr.  
 SOURCE: J. Pharmacol. Exp. Ther. (1995), 273(3), 1032-46  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In this study, the authors used a complementary *in vivo* electrophysiologic and (*in* individual rats) neurochemical approach to characterize the actions of chem. diverse serotonin (5-HT)1A receptor ligands at central 5-HT1A autoreceptors as compared to dopamine (DA) D2 autoreceptors and presynaptic alpha-2 adrenergic receptors (ARs). The novel, high efficacy 5-HT1A agonists, WAY 100,135 (an arylpiperazine), (+)-flesinoxan (a benzodioxane) and S 14671 and S 14506 (methoxyphenylpiperazines) mimicked the amantadetratin, 8-hydroxy-2-(di-n-propylamino)tetralin hydrobromide (8-OH-DPAT), in inhibiting the firing of dorsal raphe nucleus (DRN) neurons. Similarly, the firing rate of DRN neurons was reduced by the "partial" agonists, MDL 73005E, RMY 7378, NAN-190, tandospirone and the novel pyrimidinylpiperazine, zalospirone. Furthermore, S 14489, S 15535 and S 15931, novel benzodioxopiperazines, which behaved as antagonists at postsynaptic 5-HT1A receptors, inhibited completely DRN firing, whereas the methoxyphenylpiperazine, WAY 100,135, and the arylxarylamine, (-)-tertatalol, were ineffective. Indeed, in analogy to spiperone, both WAY 100,135 and (-)-tertatalol behaved as apparently competitive antagonists in that, in their presence, the dose-response curves for inhibition of DRN firing by S 14671, S 14506 or 8-OH-DPAT were shifted in parallel to the right with no loss of maximal effect. In distinction to WAY 100,135 and (-)-tertatalol, a further novel, putative "antagonist," SDZ 216-525 (a benzoisothiazolpiperazine) weakly inhibited the elec. activity of the DRN. With the exception of (-)-tertatalol, which behaved as a weak agonist, a very similar pattern of inhibition of 5-HT turnover was seen in the striatum (innervated by the DRN), the hippocampus and the hypothalamus (DRN and median raphe nucleus) and the spinal cord (nucleus raphe magnus), with the striatum displaying the

L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 greatest sensitivity. Drug potency for inhibition of firing and turnover was highly correlated ( $r = 0.80-0.82$ ) and these actions were significantly correlated to affinity at (hippocampal) 5-HT1A receptors ( $r = 0.62-0.73$ ). As concerns DA D2 autoreceptors, the agonist action of apomorphine in reducing DA turnover were mimicked only by 8-OH-DPAT, whereas the majority of the other 5-HT1A ligands, in analogy to raclopride, enhanced DA turnover. The facilitation of DA turnover appeared to reflect direct blockage of DA D2 autoreceptors because potency was correlated powerfully to affinity at these D2 sites ( $r = 0.89$ ). None of the 5-HT1A ligands mimicked the agonist action of cloridinium at alpha-2 AR autoreceptors, whereas the turnover-enhancing actions of the alpha-2 AR antagonists, idazoxan and 1-(2-pyrimidinyl)piperazine, were mimicked by many 5-HT1A ligands. Their potency did not, however, correlate with their affinity at alpha-2 ARs ( $r = 0.13$ ), probably because the alpha-2 AR antagonist actions of several ligands reflect their metab. to 1-(2-pyrimidinyl)piperazine. In conclusion, in addn. to their agonist or antagonist actions at central 5-HT1A autoreceptors, many 5-HT1A ligands display pronounced *in vivo* actions at presynaptic DA D2 receptors and alpha-2 ARs. Nevertheless, several ligand, such as S 14671, (+)-flesinoxan, S 15535 and WAY 100,235, display marked selectivity for 5-HT1A autoreceptors and an evaluation of their potential therapeutic properties should prove of particular interest.

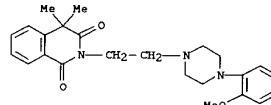
IT 23102-95-4, RMY 7378  
 RL: BAA (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (modulation of the activity of central serotonergic neurons by novel serotonergic receptor agonists and antagonists)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 132 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 DOCUMENT NUMBER: 1995:622064 CAPLUS  
 TITLE: Comparison of the binding activities of some drugs on .alpha.2A, .alpha.2B and .alpha.2C-adrenoceptors and non-adrenergic imidazoline sites in the guinea pig  
 AUTHOR(S): Uhlen, Staffan; Muceniece, Ruta; Rangel, Ninfa; Gunnar Wikberg, Jarl E. S.  
 CORPORATE SOURCE: Dep. Pharmacology, Umea Univ., Umea, S-901 87, Sweden.  
 SOURCE: Pharmacol. Toxicol. (Copenhagen) (1995), 76(6), 353-64  
 DOCUMENT TYPE: CODEN: PHTOEH; ISSN: 0901-9928  
 LANGUAGE: English  
 AB Simultaneous computer modeling of control and guanfacine-masked [3H]-MK 912 satn. curves as well as guanfacine competition curves revealed that both .alpha.2A- and .alpha.2C-adrenoceptor subtypes were present in the guinea pig cerebral cortex. The Kd value of [3H]-MK 912 detd. for the .alpha.2A-subtype was 403 pM and for the .alpha.2C-subtype 79.8 pM, the receptor sites showing capacities 172 and 19.5 fmol/mg protein, resp. The Kds of guanfacine were 20 and 880 nM for the .alpha.2A- and .alpha.2C-adrenoceptor, resp. In the guinea pig kidney [3H]-MK 912 bound to a single saturable site with Kd 8.34 nM and capacity 285 fmol/mg protein, the site showing pharmacol. properties like an .alpha.2B-adrenoceptor. Binding consts. of 22 compds. for the three guinea pig .alpha.2-adrenoceptor subtypes were detd. by computer modeling competition curves using for the cerebral cortex a "3-curve assay", for the kidney an "1-curve assay", and using [3H]-MK 912 as labeled ligand. Of the tested drugs guanfacine and BRL 4408 were found to be clearly .alpha.2A-selective. Spirokatrine, yohimbine, rauwolscine and Wb 4101, as well as [3H]-MK 912 itself, were found to be .alpha.2C-selective. The most selective compds. for .alpha.2B-adrenoceptors, when compared to .alpha.2A-adrenoceptors, were ARC 239 and prazosin. In the guinea pig kidney [3H]-p-aminoclonidine bound to .alpha.2-adrenoceptors as well as to non-adrenergic imidazoline sites. The .alpha.2-adrenoceptors could be completely blocked using 10 .mu.M (-)-adrenaline without the non-adrenergic sites being affected. During these conditions the anal. of

L14 ANSWER 132 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 combined satn. and competition studies using labeled and unlabeled p-aminoclonidine with computer modeling revealed that the ligand labeled two different sites with Kds of 310 and 47,000 nM, resp. Competition curves of 16 compds. for the non-adrenergic [3H]-p-aminoclonidine sites were shallow and resolved into two-site fits. For the high affinity [3H]-p-aminoclonidine site the highest affinities were shown by 1-medetomidine, UK-14,304, rauwolscine and atropine and the Kds of these drugs ranging 26-72 nM. All drugs tested showed low but varying affinities for the low affinity [3H]-p-aminoclonidine site. These data indicated that the [3H]-p-aminoclonidine binding sites of the guinea pig kidney are grossly different from the [3H]-idazoxan binding 12-receptors previously demonstrated also to be present in the guinea pig kidney. IT 67339-62-2, AR 239 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (comparison of drug binding on .alpha.2A, .alpha.2B and .alpha.2C-adrenoceptors and non-adrenergic imidazoline sites in guinea pig)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

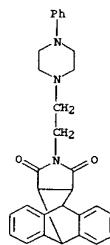


L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 DOCUMENT NUMBER: 1995:604026 CAPLUS  
 TITLE: Preparation of antiinflammatory 13-(piperazinyl)-9,10[3',4']pyrroloanthracene immunomodulators  
 INVENTOR(S): Schwenner, Eckhard; Ladouceur, Gaetan; Kabbe, Hans-Joachim; Aune, Thomas M.  
 PATENT ASSIGNEE(S): Bayer A.-G., Germany  
 SOURCE: U.S., 16 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:  

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
US 5409932	A 19950425	US 1993-164499	19931209
WO 9515946	A1 19950615	WO 1994-EP3934	19941128
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, UA, VN RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 5512411 EP 733040 R: CH, DE, FR, GB, IT, LI, JP 09506356	T2 19970624	JP 1994-515934	19941128
PRIORITY APPLN. INFO.: US 1993-164499 US 1993-164509 WO 1994-EP3934		US 1993-164499 US 1993-164509 WO 1994-EP3934	19931209 19931209 19941128

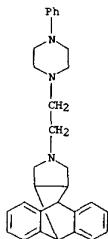
 OTHER SOURCE(S): MARPAT 123:314014  
 GI

L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 preparation; THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of antiinflammatory 13-(piperazinyl)-9,10[3',4']pyrroloanthracene immunomodulators)  
 RN 169877-39-7 CAPLUS  
 CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole-1,3(2H)-dione,  
 2a,4,9,9a-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

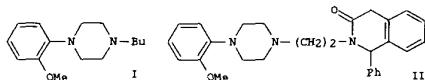


RN 169877-39-7 CAPLUS  
 CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole,  
 2,3,3a,4,9,9a-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*  
 AB The title compds. [I; A, D = H, OH, halogen, CN, CO2H, NO2, CF3, CF3O, (un)branched C1toreq.8 alkyl or alkoxy; R1, R2 = H, halogen, CN, CHO, Ph, CH, (un)substituted alkoxy, (un)substituted alkyl, (un)substituted alkenyl; R3, R4 = H, C1toreq.6 (un)branched alkyl, Ph; R5, R6 = H, halogen, Ph, (un)branched (un)substituted alkyl; R7-R10 = H, C1toreq.6 (un)branched alkyl; R11 = (un)substituted aryl; a = 0-6] (e.g., II), useful as antiinflammatories, antiarthritics, and immunosuppressives, are reported. Thus, II, m.p. 143.degree., was prep'd. and demonstrated 90% inhibition of swelling in an adjuvant arthritis rat model at 10 mg/kg (i.p.). IT 169877-38-7P 169877-92-3P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

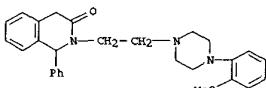


L14 ANSWER 134 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:540324 CAPLUS  
 DOCUMENT NUMBER: 123:74214  
 TITLE: Structure-activity relationship studies of CNS agents.  
 XXI: Two derivatives of 1-(o-methoxyphenyl)piperazine with an opposite function at 5-HT1A receptors  
 AUTHOR(S): Mokrosz, Jerzy L.; Kłodzinska, Aleksandra; Boksa, Jan;  
 CORPORATE SOURCE: Bojarski, Andrzej J.; Duszynska, Beata;  
 Pharmacology, Chojnacka-Wojcik, Ewa  
 SOURCE: Dep. Med. Chem., Lab. New Drugs Inst.  
 Polish Acad. Sci., Krakow, 31-343, Pol.  
 Arch. Pharm. (Weinheim, Ger.) (1995), 328(4), 381-3  
 DOCUMENT TYPE: CODEN: ARPMAZ; ISSN: 0365-6233  
 LANGUAGE: Journal English  
 GI



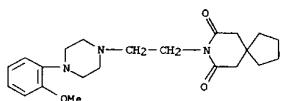
AB All postsynaptic 5-HT1A receptor antagonists which belong to the 1-arylpiperazine class of ligands have a 1-(o-methoxyphenyl)piperazine fragment or its structural equiv. (e.g. benzodioxane moiety) in their structure. Mol. modeling and structure activity studies were conducted by using model compds. I and II to substantiate the hypothesis that 1-(o-methoxyphenyl)piperazine moiety is necessary for the 5-HT1A receptor antagonist activity. Comparison of the 5-HT1A/5-HT2A selective ratio for I and II shows that the structure of the bioactive complex of I with 5-HT1A receptors is different from the 5-HT1A receptor complex of II. The 1-Ph, and not the 1-(o-methoxyphenyl), substituent and the N-4 piperazine atom of II form a pharmacophore which is recognized by the receptor. It may be anticipated that the structure of the specific bioactive complex of 5-HT1A receptor and 1-(o-methoxyphenyl)piperazine fragment is directly responsible for postsynaptic antagonist activity of these derivs.  
 IT 164988-55-0  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

L14 ANSWER 134 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (mol. modeling and structure activity relations of the 5-HT1A receptor antagonist (methoxyphenyl)piperazine derivs.)  
 RN 164988-55-0 CAPLUS  
 CN 3(2H)-Isoquinolinone, 1,4-dihydro-2-[2-{4-(2-methoxyphenyl)-1-piperazinyl}ethyl]-1-phenyl- (9CI) (CA INDEX NAME)



L14 ANSWER 135 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:470109 CAPLUS  
 DOCUMENT NUMBER: 122:230666  
 TITLE: Conditioned ultrasonic distress vocalizations in adult male rats as a behavioral paradigm for screening anti-panic drugs  
 AUTHOR(S): Molwijk, H. E.; van der Poel, A. M.; Mos, J.; Heyden, J. A. M.; Olivier, B.  
 CORPORATE SOURCE: CNS Pharmocol., Solvay Duphar B.V., Weesp, 1380 DA,  
 Neth.  
 SOURCE: Psychopharmacology (Berlin) (1995), 117(1), 32-40  
 DOCUMENT TYPE: CODEN: PSCHDL; ISSN: 0033-3158  
 LANGUAGE: Journal English  
 AB Rats may produce ultrasonic vocalizations (USV) in threatening situations. USV of adult male rats in assoc. with aversive stimulation was evaluated as a screening method for anxiolytic drugs. The triazobenzodiazepine alprazolam, the 5-HT uptake inhibitors fluvoxamine and clomipramine, the mixed 5-HT/NA uptake inhibitor imipramine, the full 5-HT1A receptor agonists 8-OH-DPAT and flesinoxan, the partial 5-HT1A receptor agonists buspirone, ipsapirone and BMY 7378, the .alpha.2-adrenoceptor agonist clonidine and the .alpha.2-adrenoceptor antagonist yohimbine reduced conditioned USV. The classical benzodiazepines (BZD) diazepam and chlordiazepoxide were ineffective or had a very low potency to decrease USV. The partial BZD receptor agonists bretazenil, alpidem and zolpidem, the BZD receptor antagonist flumazenil, the NA uptake inhibitors desipramine and maprotiline, and the 5-HT3 receptor antagonist ondansetron had no effect on conditioned USV. The dopamine-D2 receptor antagonist haloperidol reduced USV at a very high dose. In sep. expts. the effects of these drugs on locomotor activity were assessed. There was, however, no direct relation between effects on motor behavior and USV. In conclusion, the sensitivity of conditioned USV to 5-HT uptake inhibitors and alprazolam vs. the insensitivity to classical benzodiazepines and NA uptake inhibitors provides a very interesting profile, which closely resembles the psychopharmacol. of panic disorder. Also the face validity of conditioned USV towards situational panic attacks is high. We therefore propose conditioned USV in adult male rats as a novel behavioral paradigm to screen for anti-panic drugs.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); THU

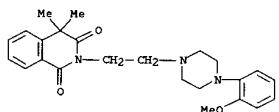
L14 ANSWER 135 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (conditioned ultrasonic distress vocalizations in adult male rats  
 as a behavioral paradigm for screening antipanic drugs)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



•2 HCl

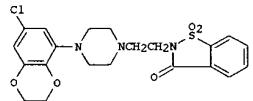
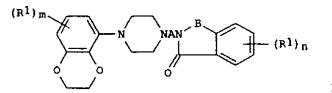
L14 ANSWER 136 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:466931 CAPLUS  
 DOCUMENT NUMBER: 122:230657  
 TITLE: Pharmacological antagonism of .alpha.-adrenergic agonist induced increases in canine intraurethral pressure in vivo  
 AUTHOR(S): Brune, Michael E.; Buckner, Steven A.; Polakowski, James; Kerwin, James F., Jr.; Hancock, Arthur A.  
 CORPORATE SOURCE: Pharmaceuticals Division, Abbott Laboratories, Abbott Park, IL, USA  
 SOURCE: Drug Dev. Res. (1995), 34(3), 267-75  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Treatment with .alpha.1 antagonists represents a pharmacological alternative to surgery for the treatment of urinary obstruction associated with benign prostatic hyperplasia (BPH). A minimally invasive method to measure elevation of prostatic urethral tone through a urethral catheter was used to study the effects of .alpha.-adrenoceptor agonists and antagonists on canine intraurethral pressure (IUP). .alpha.1-Adrenoceptor agonists, but not .alpha.2 agonists, elicited elevations in IUP. The contractile response was primarily the result of prostatic smooth muscle contraction, since it was of smaller magnitude in female dogs or in male dogs outside of the prostatic urethra. The contractile responses to epinephrine obtained in the absence of antagonist on the same or different test dates were highly reproducible in dogs greater than 2 yr of age. The increase in IUP caused by epinephrine was specifically antagonized by .alpha.1-adrenoceptor antagonists, in direct proportion to their potency in isolated canine prostatic strips in vitro and in proportion to their affinity at receptors detected in radioligand binding assays in vitro. These data confirm the role of .alpha.1-adrenoceptors in canine prostatic smooth muscle contraction and this relatively non-invasive in vivo model will allow the study of novel compounds for their effects on canine prostatic tone.  
 IT 67339-62-2, AR-C 239  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses); (pharmacol. antagonist of .alpha.-adrenergic agonist induced increases in canine intraurethral pressure in vivo)  
 RN 67339-62-2 CAPLUS  
 CN 1,3-(2H,4H)-Isquoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 136 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 137 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:422800 CAPLUS  
 DOCUMENT NUMBER: 122:187611  
 TITLE: Preparation of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivatives having 5-HT1A-antagonistic activity  
 INVENTOR(S): Hartog, Jan; Van Steen, B. J.; Mos, Johannes;  
 Schipper, Jacques  
 PATENT ASSIGNEE(S): Duphar International Research B.V., Neth.  
 SOURCE: Eur. Pat. Appl., 16 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 633260	A1	19950111	EP 1994-201900	19940701
EP 633260	B1	20011107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2127084	AA	19950106	CA 1994-2127084	19940629
FI 9403149	A	19950106	FI 1994-3149	19940630
NO 9402471	A	19950106	NO 1994-2471	19940630
JP 07215972	A2	19950815	JP 1994-170370	19940630
US 5462942	A	19951031	US 1994-269086	19940630
HU 210255	A2	19970428	HU 1994-1965	19940630
HU 210255	B	20000628		
CZ 286503	B6	20010212	CZ 1994-1597	19940630
SK 281691	B6	20010211	SK 1994-788	19940630
ZA 9404787	A	19950220	ZA 1994-4787	19940701
CN 1106813	A	19950816	CN 1994-115999	19940701
CN 1044244	B	19990721		
AT 208385	E	20011115	AT 1994-201900	19940701
ES 2167346	T3	20020516	ES 1994-201900	19940701
AU 9466139	A1	19950112	AU 1994-66139	19940704
AU 680900	B2	19970814		
RU 2118322	C1	19980827	RU 1994-23250	19940704
IL 110209	A1	20000229	IL 1994-110209	19940704
PRIORITY APPLN. INFO.:			EP 1993-201950	A 19930705
OTHER SOURCE(S):			CASREACT 122:187611; MARPAT 122:187611	GI



AB Title compds. (I; R1 = halo, lower alkyl, alkoxy, OH, CF<sub>3</sub>, cyano; m = 1,2; n = 0,1; A = C2-6 alkylene which may be substituted with .gtoreq.1 lower alkyl groups or a monocyclic (hetero)aryl group; B = CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, CO, S, SO, SO<sub>2</sub>), were prepd. Thus, saccharin was heated with

1-(7-chloro-2,3-dihydro-1,4-benzodioxin-5-yl)-4-(2-chloroethyl)piperazine and NaH in DMF to give title compd. (II). In general I were selective for 5-HT<sub>1A</sub> receptors, antagonize the effects of 8-OH-DPAT in rats, and have good oral bioavailability.

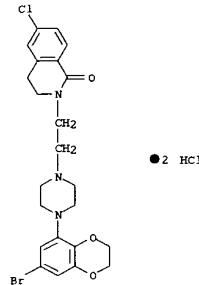
IT 161612-04-09  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivs. having 5-HT<sub>1A</sub>-antagonistic activity)

RN 161612-04-0 CAPLUS

CN 1(2H)-Isoquinolinone,

2-[2-[4-(7-bromo-2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1995:376590 CAPLUS

DOCUMENT NUMBER: 122:214029

TITLE: Structure of N-[2-(4-phenyl-1-

piperazinyl)ethyl]phthalimide

AUTHOR(S): Andronat, S. A.; Simonov, Yu. A.; Dvorkin, A.

A.: Bondarev, M. L.; Yavorsky, A. S.; Chumakov, Yu.

M. CORPORATE SOURCE: Fiz.-Khim. Inst. im. A.V. Bogatskagi, Odessa, Ukraine

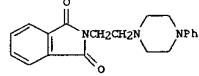
SOURCE: Dopov. Akad. Nauk Ukr. (1993), (11), 136-40

DOCUMENT TYPE: CODEN: DNUKEM

Journal

LANGUAGE: Russian

GI



AB The structure of the title compd. (I) was detd. by x-ray anal. The distance from the center of the Ph ring to the center of the phthalimide moiety was 9.90 ANG.. This distance is comparable with that in Humber's model for the dopamine receptor site. Quantum-chem. calcns., along with x-ray data, confirm that the lone electron pair of N-4 of the piperazine fragment is conjugated with the Ph ring.

IT 75000-24-7

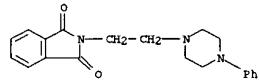
RL: PRP (Properties)

(x-ray anal. of)

RN 75000-24-7 CAPLUS

CN 1H-Isocindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-

(9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1995:320486 CAPLUS

DOCUMENT NUMBER: 122:97160

TITLE: EMY 7378 is a selective antagonist of the D

subtype of

.alpha.1-adrenoceptors

AUTHOR(S): Goetz, Aaron S.; King, Holly K.; Ward, Stuart D.

C.: True, Timothy A.; Rimele, Thomas J.; Saussy,,

David L.

CORPORATE SOURCE: JR. Department of Cellular Biochemistry, Glaxo Research Institute, Five Moore Drive, Research Triangle Park,

SOURCE: NC, 27709, USA Eur. J. Pharmacol. (1995), 272(2/3), R5-R6

DOCUMENT TYPE: CODEN: EJPHAZL ISBN: 0014-2999

LANGUAGE: English AB EMY 7378 (8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride), a 5-HT<sub>1A</sub> receptor partial agonist, also binds to .alpha.1-adrenoceptors. Competition assays were performed using (+,-)-beta-((125I)iodo-4-hydroxyphenyl)-ethyl-aminomethyl-tetralone ([125I]HEAT), and membranes prepd. from Rat-1 fibroblasts expressing hamster .alpha.1b-, bovine .alpha.1c-, or rat .alpha.1d-adrenoceptor, or their resp. human homologues. Results indicate that EMY 7378 is selective for the .alpha.1D-adrenoceptor subtype

(pKi: hamster .alpha.1b-adrenoceptor 6.2+-0.03, human

.alpha.1b-adrenoceptor

7.2+-0.05; bovine .alpha.1c-adrenoceptor 6.1+-0.02, human .alpha.1c-adrenoceptor 6.6+-0.20; rat .alpha.1d-adrenoceptor 8.2+-0.06, human .alpha.1d-adrenoceptor 9.4+-0.05) and has high affinity (pA<sub>2</sub>: 8.9+-0.1) for rat aorta .alpha.1-adrenoceptor.

IT 21102-95-4 EMY 7378

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

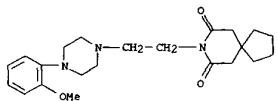
(EMY 7378 is selective antagonist of D subtype of .alpha.1-

adrenoceptor)

RN 21102-95-4 CAPLUS

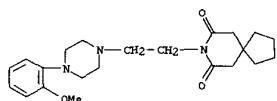
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-

piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



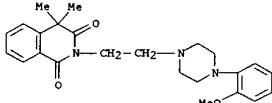
●2 HCl

L14 ANSWER 140 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:252067 CAPLUS  
 DOCUMENT NUMBER: 122:24395  
 TITLE: Differential sensitivity of 3H-agonist binding to pre- and postsynaptic 5-HT1A receptors in bovine brain  
 AUTHOR(S): Iben, Lawrence G.; Mahle, Cathy D.; Yocca, Frank D.  
 CORPORATE SOURCE: Psychobiol. Disorders, Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492, USA  
 SOURCE: Br. J. Pharmacol. (1994), 113(4), 1400-6  
 CODEN: BJPCBM; ISSN: 0007-1188  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The full and weak partial 5-HT1A agonist ligands [<sup>3</sup>H]-8-OH-DPAT and [<sup>3</sup>H]-BMY-7378 were used to characterize the binding parameters of pre- and postsynaptic 5-HT1A binding sites in bovine dorsal raphe and hippocampal membranes, resp. The K<sub>d</sub> and B<sub>max</sub> values for the individual radioligands were indistinguishable across the regions tested, as were the K<sub>i</sub> values generated by a series of agents acting at 5-hydroxytryptamine (5-HT) receptors. The concn.-dependent allosteric attenuation of [<sup>3</sup>H]-8-OH-DPAT and [<sup>3</sup>H]-BMY-7378 binding produced by the nonhydrolyzable guanyl nucleotide, Gpp(NH)p, generated similar IC<sub>50</sub> values within a particular region; however, these were significantly different between regions. While the maximal attenuation of [<sup>3</sup>H]-8-OH-DPAT and [<sup>3</sup>H]-BMY-7378 binding was similar in dorsal raphe, Gpp(NH)p produced a significantly greater attenuation of [<sup>3</sup>H]-8-OH-DPAT binding in hippocampal membranes when compared to [<sup>3</sup>H]-BMY-7378. The maximal attenuation of [<sup>3</sup>H]-8-OH-DPAT binding by Gpp(NH)p in hippocampus was also significantly greater than that seen with either radioligand in dorsal raphe. Although exposure to Gpp(NH)p had no effect on the affinity consts. of either radioligand in either region, it produced a concn.-dependent redn. in the maximal no. of binding sites for both radioligands in both regions. While the percentage redn. in B<sub>max</sub> values were similar for both radioligands in the dorsal raphe, Gpp(NH)p reduced the B<sub>max</sub> of [<sup>3</sup>H]-8-OH-DPAT in the hippocampus significantly more than that of [<sup>3</sup>H]-BMY-7378. These results suggest that while pre- and postsynaptic 5-HT1A receptors may share similar pharmacol. recognition properties, a region-dependent difference in the coupling of the 5-HT1A receptor to G-proteins may exist.  
 IT 21102-95-4, BMY-7378  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (serotonin pre- and postsynaptic 5IA receptor ligand binding similarity)

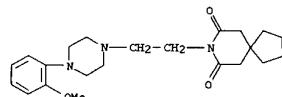


●2 HCl

L14 ANSWER 141 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:247986 CAPLUS  
 DOCUMENT NUMBER: 122:24361  
 TITLE: Species orthologs of the alpha-2A adrenergic receptor:  
 receptors differ from the human and porcine  
 rat receptors  
 AUTHOR(S): O'Rourke, M. F.; Iversen, L. J.; Lomasney, J. W.; Bylund, D. B.  
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Nebraska Med. Cent., Omaha, NE, USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1994), 271(2), 735-40  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Four pharmacol. subtypes of the alpha-2 adrenergic receptor have been identified; however, only three subtypes exist in any given species. Although the alpha-2A adrenergic receptor, as defined by the human platelet, and the alpha-2D receptor, as defined in the bovine pineal, have very different pharmacol. characteristics, they are more similar to each other than either is to the alpha-2B or alpha-2C subtype. The human alpha-2-C10 clone (alpha-2A) and the rat RG20 clone have an 89% identity in their predicted amino acid sequence and are considered to be species orthologs. Although the expressed RG20 clone appears to have alpha-2D pharmacol., a careful comparison of its pharmacol. characteristics with the bovine pineal has not been reported previously. Based on the pK<sub>i</sub> values of a panel of 13 alpha-2 adrenergic agents that have been used previously to compare the alpha-2A, alpha-2B and alpha-2C subtypes, the pharmacol. characteristics of the bovine pineal alpha-2D receptor appear to be very similar to the rat RG20 clone (correlation coeff., r, of 0.93). The porcine ortholog of the human alpha-2-C10 receptor has pharmacol. characteristics identical to the human alpha-2A receptor ( $r = 0.99$ ). Because of its higher affinity for the alpha-2D receptor, [<sup>3</sup>H]RX 82100 is a better radioligand than [<sup>3</sup>H]rauwolscine for studying this receptor subtype.  
 IT 67339-62-2, ARC 239  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (pharmacol. of .alpha.2A-adrenergic receptor of bovine and rat differ from human and receptors)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-dimethyl- (9CI) (CA INDEX NAME)

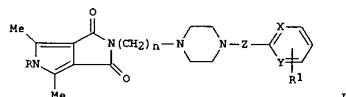


L14 ANSWER 142 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:225638 CAPLUS  
 DOCUMENT NUMBER: 122:1607  
 TITLE: Serotonin inhibition of adenylyl cyclase in human platelet membranes; relation to 5-HT<sub>1A</sub> receptor-mediated activity  
 AUTHOR(S): Newman, Michael E.  
 CORPORATE SOURCE: Dep. Psychiat., Hadassah Univ. Hosp., Jerusalem, Israel  
 SOURCE: Biochemical Pharmacology (1994), 48(9), 1677-82  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Serotonin inhibited both basal and forskolin-stimulated adenylyl cyclase activity in human platelet membranes by approx. 30%, with an EC<sub>50</sub> of 54 nM. Addn. of NaCl to the assay medium reduced the degree of inhibition. 5-Carboxamidotryptamine (5-CT) behaved as a full agonist in this system (EC<sub>50</sub> of 5.4 nM) and BMY 7378 and a partial agonist (inducing 19% inhibition); the putative 5-HT<sub>1A</sub> receptor agonists metergoline, spiroxatrine and MDL 73005 were inactive. The 5-HT<sub>1A</sub> receptor antagonists mirtazapine and NAN-190 behaved as antagonists with K<sub>i</sub> or K<sub>d</sub> values of 11.2 and 1.17 nM, resp. Spiperone behaved as a partial antagonist only. Epinephrine and 5-HT produced convergent, nonadditive inhibition of both basal and forskolin-stimulated cyclase.  
 IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (serotonin inhibition of adenylyl cyclase in human platelet membranes in relation to serotoninergic S1A receptor)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapipro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

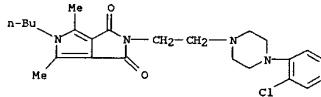


●2 HCl

L14 ANSWER 143 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:84779 CAPLUS  
 DOCUMENT NUMBER: 123:9354  
 TITLE: Synthesis and biological evaluation of derivatives of N-[4-substituted-1-piperazinylalkyl]-1-(butyl, aryl)-2,5-dimethylpyrrole-3,4-dicarboximide (Part II)  
 AUTHOR(S): Malinka, Wieslaw; Sieklucka-Dziuba, Maria; Robak, Jacek; Kleinrok, Zdzislaw  
 CORPORATE SOURCE: Dep. Drugs Chem., Medical Acad., Wroclaw, 50-137, Pol.  
 SOURCE: Farmaco (1994), 49(7-8), 481-7  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

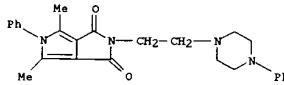


AB The title compds. I (n = 2-4; X, Y = CH, N; Z = -, CH<sub>2</sub>; R = Bu, Ph, 2-MeC<sub>6</sub>H<sub>5</sub>; R1 = H, Cl) have been prepd. by reaction of N-haloalkylimide derivs. with the corresponding N-monosubstituted piperazines. I were tested in preliminary pharmacol. investigations, and produced a general depressive action on the central nervous system.  
 IT 159658-13-6P 159658-14-7P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (pyrrole-3,4-dicarboximides)  
 RN 159658-13-6 CAPLUS  
 CN Pyrrole[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-1-2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

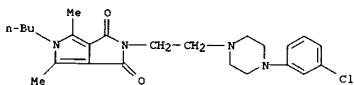


RN 159658-14-7 CAPLUS

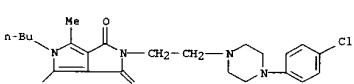
L14 ANSWER 143 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN Pyrrole[3,4-c]pyrrole-1,3(2H,5H)-dione,  
 4,6-dimethyl-5-phenyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



IT 159658-19-2P 159658-20-5P  
 RL: SPM (Synthetic preparation); PREP (Preparation)  
 (prepa. and CNS activity of  
 (piperazinylalkyl)pyrroledicarboximides)  
 RN 159658-19-2 CAPLUS  
 CN Pyrrole[3,4-c]pyrrole-1,3(2H,5H)-dione,  
 5-butyl-2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

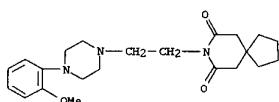


RN 159658-20-5 CAPLUS  
 CN Pyrrole[3,4-c]pyrrole-1,3(2H,5H)-dione,  
 5-butyl-2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 144 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 190 and propranolol on serotonergic dorsal raphe unit activity in  
 behaving cats

RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 144 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:692532 CAPLUS  
 DOCUMENT NUMBER: 121:292532  
 TITLE: Effects of the putative 5-hydroxytryptamineA antagonists BMY 7378, NAN 190 and (-)-propranolol  
 on serotonergic dorsal raphe unit activity in

behaving cats  
 AUTHOR(S): Fornal, Casimir A.; Marrosu, Francois Metzler,  
 Christine W.; Tada, Koji; Jacobs, Barry L.  
 CORPORATE SOURCE: Dep. Physiol., Princeton Univ., Princeton, NJ, USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1994), 270(3), 1359-66  
 CODEN: JPETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Recent evidence from the authors lab. has demonstrated that blockade  
 of somatodendritic 5-hydroxytryptamine (5-HT1A) autoreceptors by systemic  
 administration of spiperone increases the firing rate of central  
 serotonergic neurons in awake cats. The present study exams the  
 effects of 3 other putative 5-HT1A antagonists (BMY 7378 (8-[2-[4-(2-

methoxyphenyl)-1-piperazinyl]ethyl)-8-azaspiro[4.5]-decano-7,9-dione), NAN  
 190 ((2-methoxyphenyl)-4-[4-(2-phthalimidobutyl)piperazine) and  
 (-)-propranolol on the single-unit activity of serotonergic neurons  
 recorded in the dorsal raphe nucleus of free-moving cats. Systemic  
 administration of the phenylpiperazine derivs. BMY 7378 (5-100  
 .mu.g/kg i.v.) and NAN 190 (5-250 .mu.g/kg i.v.) produced a rapid,  
 dose-dependent inhibition of neuronal activity with BMY 7378 being approx. twice as  
 potent as NAN 190 (ED50 = 15.3 .mu.g/kg vs. 34.2 .mu.g/kg). The  
 suppression of neuronal activity produced by both compds. was greatly attenuated by spiperone (1 mg/kg i.v.). Systemic administration of  
 (-)-propranolol (2 and 4 mg/kg i.v.) produced a modest suppression of  
 serotonergic neuronal activity which did not appear to be

dose-dependent. The ability of BMY 7378, NAN 190 and (-)-propranolol to block the  
 suppression of neuronal activity produced by 8-hydroxy-2-(di-n-  
 propylamino)tetralin (8-OH-DPAT), a selective 5-HT1A agonist, was also  
 exams. Pretreatment with these compds. had no significant effect on  
 the inhibitory response of serotonergic neurons to 8-OH-DPAT challenge.

These results indicate that BMY 7378 and NAN 190 act as agonists rather than  
 antagonists at the somatodendritic 5-HT1A autoreceptor. Furthermore,  
 (-)-propranolol, unlike spiperone, does not appear to be an effective  
 5-HT1A autoreceptor antagonist, because it did not block the action  
 8-OH-DPAT or increase basal serotonergic neuronal activity in awake  
 animals.

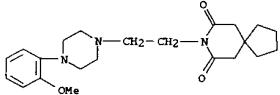
IT 21102-95-4, BMY 7378  
 RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)  
 (effects of putative 5-hydroxytryptamineA antagonists BMY 7378  
 and NAN

L14 ANSWER 145 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:536576 CAPLUS  
 DOCUMENT NUMBER: 121:196576  
 TITLE: Serotonin and pain: Evidence that activation of  
 5-HT1A receptors does not elicit antinociception against  
 noxious thermal, mechanical and chemical stimuli

in mice  
 AUTHOR(S): Millan, Mark J.  
 CORPORATE SOURCE: Institut de Recherches Servier, Puteaux, 92800,  
 Fr.  
 SOURCE: Pain (1994), 58(1), 45-61  
 CODEN: PAINDB; ISSN: 0304-3959

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In this study, we exams. whether activation of 5-HT1A receptors  
 elicits antinociception in response to acute noxious chem., thermal and mech.  
 stimuli in mice. In the writhing test, both agonists (e.g.,  
 8-OH-DPAT, S 14671 and WY 50,324) and partial agonists (e.g., buspirone and  
 gepirone) elicited a pronounced antinociception. However, antagonists (e.g.,  
 (-)-alprenolol and WAY 100,135) also induced antinociception and, at  
 lower (inactive) doses, failed to modify the action of agonists. In addn.,  
 the sep. between doses required for induction of antinociception as  
 compared to those required for induction of ataxia (in the rotarod test) was  
 variable and low for both agonists (median: 1.9) and partial agonists  
 (median: 1.3), although it was somewhat greater for antagonists  
 (.gtreq.3.3). In the hot-plate test, only certain agonists (e.g.,  
 8-OH-DPAT) and partial agonists (e.g., gepirone) elicited  
 antinociception and their actions were not attenuated by 5-HT1A antagonists which,  
 themselves, were inactive in this paradigm. The 5-HT1C/2 antagonist,  
 ritanserin, the 5-HT3 antagonist, ondansetron, the dopamine D2  
 receptor antagonist, raclopride, and the .alpha.1-adrenoceptor antagonist,  
 prazosin, were also ineffective in modifying the antinociception  
 evoked by 5-HT1A agonists and partial agonists in the hot-plate test. In  
 contrast, their actions were strongly attenuated by the .alpha.2-adrenoceptor  
 antagonist, idazoxan. In the tail-flick tests to noxious heat and  
 noxious pressure, 5-HT1A receptor agonists, partial agonists and antagonists  
 generally failed to induce antinociception. Moreover, modulation of  
 stimulus intensity (from very weak to very intense) did not reveal any  
 influence upon the latency to respond. In conclusion, in the writhing  
 test, the data provide no evidence for a specific antinociceptive  
 effect of the activation of 5-HT1A receptors. Further, in the hot-plate  
 test, for those 5-HT1A agonists and partial agonists which induce

L14 ANSWER 145 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 antinociception, .alpha.2-adrenoceptors rather than 5-HT1A receptors are implicated in their actions. Finally, in reflexive tests, irresp. of stimulus quality or intensity, 5-HT1A agonists and partial agonists do not mediate antinociception. These data suggest that the activation of 5-HT1A receptors does not, under these conditions of acute noxious stimulation, elicit antinociception.  
 IT 21102-95-4, RMY 7378  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antinociception against noxious thermal, mech. and chem. stimuli in mice)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

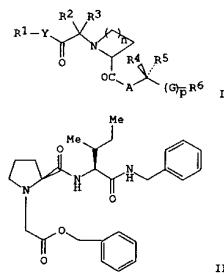


●2 HCl

L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 1994:509676 CAPLUS  
 DOCUMENT NUMBER: 121:109676  
 TITLE: Preparation of N-(2-oxethyl)amino acid derivatives  
 INVENTOR(S): Michael Connell, Richard D.; Osterman, David D.; Katz, E.  
 PATENT ASSIGNEE(S): Miles Inc., USA  
 SOURCE: Eur. Pat. Appl., 96 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 564924	A2	19931013	EP 1993-105035	19930326
EP 564924	A3	19931229		
EP 564924	B1	19980909		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2091194	AA	19931009	CA 1993-2091194	19930308
AT 170870	E	19980915	AT 1993-105035	19930326
ES 2119826	T3	19981016	ES 1993-105035	19930326
AU 9336773	A1	19931014	AU 1993-36773	19930406
AU 666179	B2	19960201		
JP 06041064	A2	19940215	JP 1993-106160	19930408
US 5666424	A	19971111	US 1995-431390	19950428
PRIORITY APPLN. INFO.:			US 1992-864998	19920408
OTHER SOURCE(S): MARPAT 121:109676			US 1992-991565	19921125
GI				

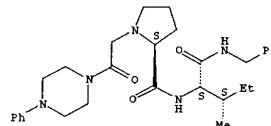
L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Title compds. I [R1 = H, (un)substituted alkyl, (un)substituted alkenyl, cycloalkyl, etc.; Y = bond, O, (un)substituted imino; R1-Y = (un)substituted heterocycl; one of R2 and R3 = H and the other = alkyl; n = 2, 3; A = O, (un)substituted imino; R4, R5 = H, (un)substituted alkyl, etc.; G = CH:CH<sub>2</sub>, CH<sub>2</sub>-CH<sub>2</sub>, NHCO; R6 = H, (un)substituted alkyl, (un)substituted Ph, etc.; p = 0, 1] are prep'd. E.g., L-proline-L-isoleucine benzylamide (prepn. given) in MeCN was refluxed with benzyl 2-bromoacetate to give the title compd. II. In an *in vitro* study, this had an IC<sub>50</sub> of 2.2 .mu.M against peptidyl prolyl isomerase.  
 IT 156800-43-0P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prep. of, as immunosuppressant)  
 RN 156800-43-0 CAPLUS  
 CN L-isoleucinamide,  
 1-(2-oxo-2-(4-phenyl-1-piperazinyl)ethyl)-L-prolyl-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

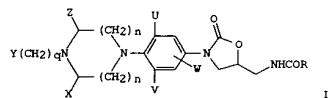
L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994-323599 CAPLUS  
 DOCUMENT NUMBER: 120:323599  
 TITLE: Oxazolidinones antibiotics containing a substituted diazine moiety  
 INVENTOR(S): Hutchinson, Douglas K.; Brickner, Steven Joseph; Barbachyn, Michael Robert; Gammill, Ronald B.; Patel, Mahesh V.  
 PATENT ASSIGNEE(S): Upjohn Co., USA  
 SOURCE: PCT Int. Appl., 44 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:  

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323384	A1	19931125	WO 1993-US3570	19930421
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KR, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GE, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342877	A1	19931213	AU 1993-42877	19930421
AU 668733	B2	19960516		
EP 640077	A1	19950301	EP 1993-912267	19930421
EP 640077	B1	20020626		
R: AT, BE, CH, DE, DK, ES, FR, GE, GR, IE, IT, LI, LU, MC, NL, PT, PT				
JP 07506829	T2	19950727	JP 1993-520226	19930421
JP 3255920	B2	20020212		
HU 72296	A2	19960429	HU 1994-3208	19930421
CZ 281884	B6	19970312	CZ 1994-2505	19930421
HU 2100003	C1	19980220	RU 1994-4601	19930421
PL 174950	B1	19981030	PL 1993-31588	19930421
PL 174909	B1	19981030	PL 1993-306030	19930421
AT 219770	E	20020715	AT 1993-912267	19930421
ZA 9302855	A	19941024	ZA 1993-2855	19930422
IL 105555	A1	19980715	IL 1993-105555	19930429
CN 1079964	A	19931229	CN 1993-105039	19930508
CN 1044236	B	19990721		
NO 9404237	A	19950104	NO 1994-4237	19941107
FI 9405246	A	19941108	FI 1994-5246	19941108
PRIORITY APPN. INFO.:		US 1992-880432	A1 19920508	
		WO 1993-US3570	A 19930421	
OTHER SOURCE(S):	MARPAT 120:323599			
GI				

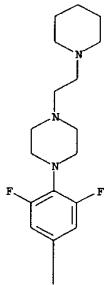
L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title compds. [I]: R = H, (un)substituted C1-6 alkyl, C3-12 cycloalkyl, C1-6 alkoxy, etc.; U, V, W = (un)substituted C1-6 alkyl, F, Cl, Br, H; X = Z = C1-6 alkyl, C3-12 cycloalkyl, H; Y = H, C1-6 alkyl, aryl, OH, (un)substituted PhO, (un)substituted piperidino, etc.; effective against members of human and veterinary pathogens, including multiple-drug-resistant *Staphylococci*, *Streptococci*, anaerobic organisms such as *Bacteroides* and *Clostridia*, and acid-fast organisms such as *Mycobacterium tuberculosis* and *Mycobacterium avium*, are prep'd. Thus, Me 4-[4-(5-(acetamino)methyl)-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-piperazinecarboxylate, prep'd. from 3,4-difluoroniobenzene in 12 steps, demonstrated 50% oral ED in the Murine Assay procedure using female mice infected with *S. aureus* (UC# 6685) of 4.0 mg/kg, vs. 6.6 for ciprofloxacin. IT 154590-81-5 154590-90-6 RL: RCT (Reactant) (prep'n. as antibiotic) RN 154590-81-5 CAPLUS CN Acetamide, N-[(3-[3,5-difluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl)methyl]-, (S)- (CA INDEX NAME)  
Absolute stereochemistry.

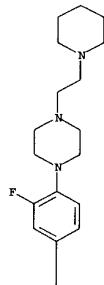
L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

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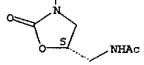


L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

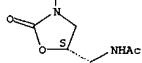
PAGE 1-A



PAGE 2-A



PAGE 2-A

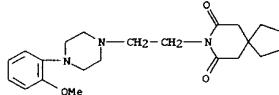


RN 154590-90-6 CAPLUS  
 CN Acetamide, N-[(3-[3-fluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl)methyl]-, (S)- (CA INDEX NAME)

Absolute stereochemistry.

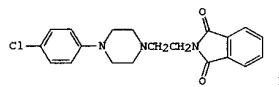
L14 ANSWER 148 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:316528 CAPLUS  
 DOCUMENT NUMBER: 120:316528  
 TITLE: Differential effects of N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) on various 5-HT receptor binding sites in the rat brain  
 AUTHOR(S): Gozlan, H.; Laporte, A. M.; Thibault, S.; Schechter, L. E.; Bolanos, F.; Hamon, M.  
 CORPORATE SOURCE: INSERM U 288/Neurobiol. Cell. Fonctionnelle, Fac. Med.  
 SOURCE: Pitie-Salpetriere, Paris, 75634, Fr.  
 Neuropharmacology (1994), 33(3-4), 423-31  
 CODEN: NEPHW; ISSN: 0028-3908  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ), an alkylating agent producing irreversible blockade of various membrane bound receptors in brain, were investigated on four different types of serotonin receptors, 5-HT1A, 5-HT1B, 5-HT2A and 5-HT3, in various brain regions in the rat. In addn., the fate of central benzodiazepine- and R-zacopride-specific binding sites was also examed. In rats treated with EEDQ, Membrane binding assays and/or quant. autoradiog. with appropriate radioligands indicated that EEDQ inactivated 5-HT1A, 5-HT1B and 5-HT2A sites, but was poorly active on 5-HT3, benzodiazepine and "R" sites. Among the receptors affected by EEDQ, hippocampal 5-HT1A sites were the most sensitive to the alkylating agent (LD50.apprx.1 mg/kg i.p.), followed by the cortical 5-HT2A (LD50.apprx.6 mg/kg i.p.) sites. Pretreatment by selective ligands partially protected hippocampal 5-HT1A sites from irreversible inactivation by EEDQ (10 mg/kg i.p.) with the following order of efficacy: WAY 100135 > spiperone > RMY 7378 > ipsapirone. Similarly, pretreatment by spiperone (5 mg/kg i.p.) also reduced the ability of EEDQ to inactivate cortical 5-HT2A receptors. Analyses of the time-course recovery of resp. binding sites after EEDQ administration showed that the turnover rate of 5-HT1A sites did not significantly differ in the dorsal raphe nucleus and in various forebrain areas (hippocampus, septum, cerebral cortex; half-life.apprx.4 days), but was lower than that of cortical 5-HT2A sites (half-life: 2.9 days).  
 IT 21102-95-4, RMY 7378  
 RL: BIOL (Biological study)  
 (serotonin receptor binding by, receptor inactivation by EEDQ

L14 ANSWER 148 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 prevention by, in brain)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



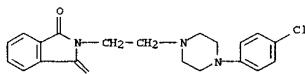
●2 HCl

L14 ANSWER 149 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:261043 CAPLUS  
 DOCUMENT NUMBER: 120:261043  
 TITLE: Long lasting inhibition of food intake in the rat by a new phthalimidoethylpiperazine derivative  
 AUTHOR(S): Mustafa, A. A.; Al-Rashid, K. A.; El-Obeid, H. A.  
 CORPORATE SOURCE: Coll. Med., King Saud Univ., Riyadh, 11461, Saudi Arabia  
 SOURCE: Res. Commun. Psychol., Psychiatry Behav. (1993), 18(1-2), 25-36  
 CODEN: RCPBDC; ISSN: 0362-2428  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB 1-[(P-Chlorophenyl)-4-(phthalimidoethyl)]piperazine (I; CPPEP), a newly synthesized compd., produced a dose-dependent inhibition of food intake in food-deprived male Wistar rats. This effect was still apparent three days after injection of the compd. The anorectic effect was not antagonized by either the non-selective 5-HT receptor antagonist, methysergide (5 mg kg<sup>-1</sup>, i.p.), nor by the 5-HT2 receptor antagonist, ketanserin (1 mg kg<sup>-1</sup>, i.p.), pindolol (4 mg kg<sup>-1</sup>, i.p.), which blocks .beta.-adrenoceptors and some of the effects mediated at 5-HT1 receptors, did not block the redn. in food intake produced by the compd. Similarly the non-selective alpha-adrenoceptor antagonist, phentolamine (5 mg kg<sup>-1</sup>, i.p.) and the alpha-2-adrenoceptor blocker, yohimbine (2 mg kg<sup>-1</sup>, i.p.) did not affect the anorectic effect of CPPEP. The hypophagic effect of CPPEP, however, was antagonized by the D2-dopamine receptor blocker, (+)-sulpiride (30 mg kg<sup>-1</sup>, i.p.) and by the relatively selective 5-HT3 receptor antagonist, zacopride (1 mg kg<sup>-1</sup>, i.p.). None of the antagonists used had any effect on food intake when they were administered alone. It is concluded that

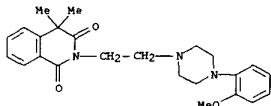
L14 ANSWER 149 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 the anorectic action of CPPEP is mediated, at least in part, by interaction with 5-HT3 receptors.  
 IT 75000-30-5  
 RL: PH (Properties)  
 (long-lasting anorectic effect of, serotoninergic 53 receptors in)  
 RN 75000-30-5 CAPLUS  
 CN 1H-1-mindole-1,3(2H)-dione,  
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-  
 (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1994:244969 CAPLUS

DOCUMENT NUMBER: 120:244969

**TITLE:** Synthesis of 1-arylpiperazine amides of 2-(4-(methoxyphenyl)-1H,5H-pyridin-2,6-dione-1-yl)acetic, -propionic acids  
**AUTHOR(S):** Thakur, K. D.; Samant, S. D.  
**CORPORATE SOURCE:** Org. Chem. Res. Lab., Univ. Dep. Chem. Technol., Dongri, Mumbai 400 019, India  
**SOURCE:** J. Indian Chem. Soc. (1993), 70(3), 261-3  
**DOCUMENT TYPE:** Journal  
**LANGUAGE:** English  
**OTHER SOURCE(S):** CASREACT 120:244969  
**GI**

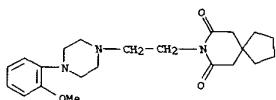


L14 ANSWER 152 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1994:96856 CAPLUS  
DOCUMENT NUMBER: 120:96856  
TITLE: Electrophysiological evidence for a large receptor reserve for inhibition of dorsal raphe neuronal firing by 5-HT1A agonists

AUTHOR(S): Cox, Richard F.; Meller, Emanuel; Waszczak, Barbara L.  
CORPORATE SOURCE: Bouve Coll. Pharm. Health Sci., Northeast. Univ., Boston, MA, 02115, USA  
SOURCE: Synapse (N. Y.) (1993), 14(4), 297-304  
CODEN: SYNABT; ISSN: 0887-4476

DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Previous studies (Meller et al. 1990) have shown that a large receptor reserve exists for the inhibition of 5-HT synthesis in rat cortex and hippocampus by the 5-HT1A agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT), whereas little or no reserve exists for the lower efficacy agonists ipsapirone and BMY 7378. The current studies were undertaken to det. if the above drugs exhibit similar relative efficacies and receptor reserves in an electrophysiolog. model of 5-HT1A receptor activation, i.e., the inhibition of dorsal raphe cell firing. I.v. dose-response curves were constructed in untreated control rats, or in rats which received an injection of the irreversible receptor inactivator N-ethoxycarbonyl-2-shoxy-1,2-dihydroquinoline (EDQ) 6 mg/kg, s.c. 24 h before recording. All 3 drugs fully inhibited dorsal raphe cell firing in control rats (ED50's: 1.5 .mu.g/kg, 8-OH-DPAT; 30.0 .mu.g/kg, ipsapirone; 17.5 .mu.g/kg, BMY 7378). However, unlike effects on 5-HT synthesis, EDQ treatments caused no depression of the maximal inhibitory response for any of the agonists, although all dose-response curves were shifted to the right (ED50's: 10.1 .mu.g/kg, 6.7-fold shift, 8-OH-DPAT; 139.9 .mu.g/kg, 4.7-fold shift, ipsapirone; 53.8 .mu.g/kg, 3.1-fold shift, BMY 7378). Although the order of agonist efficacies was similar for both inhibition of 5-HT synthesis and dorsal raphe cell firing (8-OH-DPAT > ipsapirone > BMY 7378), a large (>50%) receptor reserve was estd. for all 3 drugs in this electrophysiolog. system. This suggests that 5-HT1A receptor populations mediating the inhibition of transmitter synthesis and neuronal firing may be differently regulated or have different receptor-effector coupling characteristics (G-proteins, effectors, and/or transduction efficiencies).  
IT 21102-95-4, BMY 7378  
RL: BIOL (Biological study)

L14 ANSWER 152 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
(dorsal raphe neuron firing inhibition by, receptor reserve for serotonin formation inhibition and)  
RN 21102-95-4 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

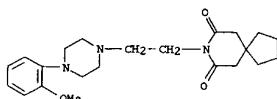


●2 HCl

L14 ANSWER 153 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1994:95766 CAPLUS  
DOCUMENT NUMBER: 120:95766  
TITLE: Preparation containing interferon-.alpha. and histamine, serotonin or substances with corresponding receptor activity for activation of natural killer cells  
INVENTOR(S): Hellstrand, Kristoffer; Hermansson, Svante  
PATENT ASSIGNEE(S): Estero-Anstalt, Liechtenstein  
SOURCE: PCT Int. Appl., 24 pp.  
CODEN: PIXX02  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324144	A1	19931209	WO 1993-SE496	19930603
W: AT, AU, BE, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, SE, SK, US, VN				
SE: KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9201719	A	19931204	SE 1992-1719	19920603
SE 513429	C2	20000911		
AU 9343660	A1	19931230	AU 1993-43660	19930603
AU 672610	B2	19961010		
EP 652768	A1	19950517	EP 1993-913731	19930603
EP 652768	B1	20000503		
PT, SE				
JP 08502024	T2	19960305	JP 1993-500471	19930603
JP 2880259	B2	19990510		
ES 2147758	T3	20001001	ES 1993-913731	19930603
US 5728378	A	19980317	US 1995-374787	19950508
PRIORITY APPLN. INFO.: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL			SE 1992-1719	A 19920603
AB Pharmaceutical preps. for activation of natural killer cells, for example in order to treat tumors or virus infections, comprises a first compn. contg. interferon-.alpha. or analogs thereof, together with a second compn. contg. at least one substance with H2 or 5-HT1a receptor agonistic activity, for example, histamine or serotonin. The first and second compns. are either mixed in a prep., or furnished in sep. doses. A combination of interferon-.alpha. and histamine showed a synergistic antitumor activity of natural killer cells against cultured target cells. IT 21102-95-4, BMY 7378 RL: BIOL (Biological study) (natural killer cell activation by .alpha.-interferon and) RN 21102-95-4 CAPLUS		WO 1993-SE496	A 19930603	

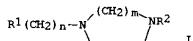
L14 ANSWER 153 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

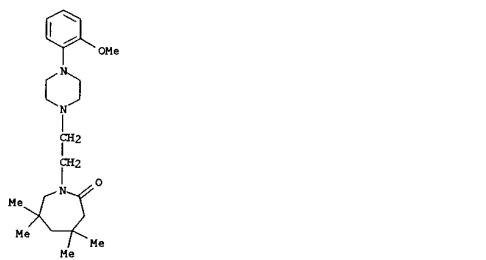
L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:77181 CAPLUS  
 DOCUMENT NUMBER: 120:77181  
 TITLE: Preparation of hexahydroazezepine derivatives as 5-HT1A serotonergic receptor antagonists  
 INVENTOR(S): Takahashi, Nobuyuki; Suzuki, Yukio; Mochizuki, Daisuke; Tsujita, Ryuchi; Yaso, Masao; Komaki, Hisayuki  
 PATENT ASSIGNEE(S): Asahi Kasei Kogyo K. K., Japan  
 SOURCE: PCT Int. Appl., 145 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9311116	A1	19930610	WO 1992-JP1533	19921124
JP 05345764	A2	19931227	JP 1992-307377	19921117
PRIORITY APPLN. INFO.:			JP 1991-336052	19911126
			JP 1992-307377	19921117
OTHER SOURCE(S):		CASREACT 120:77181; MARPAT 120:77181		
GI				



AB The title compds. (I; R1 = (un)substituted hexahydroazezepin-1-yl; R2 = (un)substituted Ph, e.g., (trifluoromethyl)phenyl, (un)substituted pyridazinyl or 1,2-benzisothiazolyl; n = 2-5 integer; m = 2, 3), 5-HT1A serotonergic receptors and therefore useful for treatment of many ailments, e.g., anxiety, depression, motion sickness, hypertension (no data), are prepd. E.g., caprolactam was treated with Cl-(CH<sub>2</sub>)<sub>3</sub>-Br in THF contg. NaH at room temp. for 5 h to give 1-(3-chloropropyl)hexahydro-1H-azezine, which was refluxed with 1-(3-(trifluoromethyl)phenyl)piperazine in benzene contg. Et<sub>3</sub>N for 139 h to give I [R1 = hexahydro-1H-azezepin-1-yl, R2 = 3-(trifluoromethyl)phenyl, n = 3, m = 2], which had an affinity (Ki) of 13.7 nM for 5-HT1A receptors.  
 IT 151142-17-5P 151142-46-0P 151142-47-1P  
 151142-48-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as serotonergic receptor antagonist)  
 RN 151142-17-5 CAPLUS

L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 2H-Azepin-2-one, hexahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4,6,6-tetramethyl- (9CI) (CA INDEX NAME)

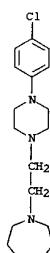


RN 151142-46-0 CAPLUS  
 CN 1H-Azepine, hexahydro-1-[2-[4-(3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

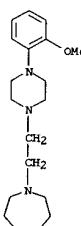


RN 151142-47-1 CAPLUS  
 CN 1H-Azepine, 1-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]hexahydro- (9CI) (CA INDEX NAME)

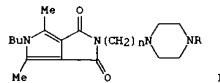
L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 151142-48-2 CAPLUS  
 CN 1H-Azepine, hexahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 155 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:45179 CAPLUS  
 DOCUMENT NUMBER: 120:45179  
 TITLE: Synthesis and pharmacological properties of N-(4-substituted-1-piperazinylalkyl)-1-butyl-2,5-dimethylpyrrole-3,3-dicarboxyimide derivatives  
 AUTHOR(S): Malinka, Wieslaw; Tarczynska, Ewa  
 CORPORATE SOURCE: Dep. Pharm., Med. Acad. Wroclaw, Wroclaw,  
 51-137, Pol.  
 SOURCE: Farmaco (1993), 48(7), 933-47  
 CODEN: FARMCE8  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



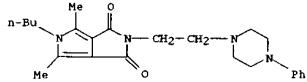
AB The prepn. of a no. of title compds. (I; R = ph, Me, pyridinyl, pyrimidinyl) is described. The structures of the novel compds. were confirmed by elemental and spectral analyses. The results of a preliminary pharmacol. study of CNS effects caused by I are presented.

IT 151722-70-2\*

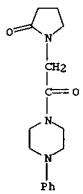
RL: BAC (Biological activity or effector, except adverse); BPR (Biological processes); SPP (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (prepn. and pharmacol. of, structure in relation to)

RN 151722-70-2 CAPLUS

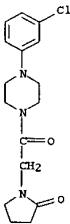
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-4,6-dimethyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



RN 131028-02-9 CAPLUS  
 CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)



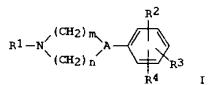
RN 135459-98-2 CAPLUS  
 CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:8615 CAPLUS  
 DOCUMENT NUMBER: 120:8615  
 INVENTOR(S): Phenyl-substituted heterocyclic antiviral agents  
 Kurono, Masayasu; Baba, Yutaka; Iwata, Noriyuki;  
 Kakigami, Takuji; Isogawa, Kogaku; Mitani,  
 Takahiko; Ishiwata, Yoshiro; Yokochi, Shoji; Otsuka,  
 Tamaki; et al.  
 SOURCE: Sanwa Kagaku Kenkyusho Co., Ltd., Japan  
 EUR. Pat. Appl., 35 pp.  
 CODEN: EPXXDW

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 548798	A1	19930630	EP 1992-121466	19921217
PT, SE	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,			
JP 150558089	A2	19931005	JP 1992-343127	19921130
OTHER SOURCE(S):	MARPAT 120:8615		JP 1991-335028	19911218



AB The title compds. I [A = N, CH2; R1 = alkyl, acyl, arylsulfonyl, acylamino, alkyl, HO, alkylxy, halogen, CO2H, NO2, cyano, SH, etc.; m = 0, natural no.; n = natural no.], useful against infectious diseases caused by

DNA viruses, RNA viruses, or retroviruses, are prep'd. Thus, 1-(2-chlorophenyl)-4-(2-pyrrolidin-1-ylacetyl)piperazine was condensed with Me 2-pyrrolidone-1-acetate, producing

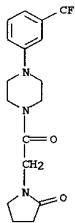
1-(2-chlorophenyl)-4-(2-pyrrolidin-1-ylacetyl)piperazine (II) in 77.1% yield. II demonstrated no tissue cytotoxicity and had antiviral activity against herpes simplex virus type 1 at 10 .mu.g/mL.

IT 131027-95-7 131028-02-9 135459-98-2

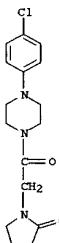
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
 (antiviral activity of)

RN 131027-95-7 CAPLUS

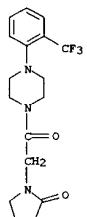
L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



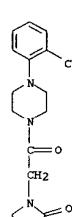
RN 150558-40-0 CAPLUS  
 CN Piperazine, 1-(4-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)



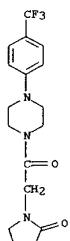
RN 150558-41-1 CAPLUS  
 CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 150558-42-2 CAPIUS  
CN Piperazine,  
1-[{(2-oxo-1-pyrrolidinyl)acetyl}-4-[4-(trifluoromethyl)phenyl]-  
(S)- (CA INDEX NAME)



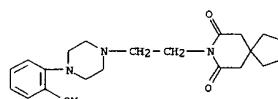
RN 150558-42-2 CAPLUS  
CN Piperazine,  
1-[ $(2\text{-}\text{oxo}-1\text{-pyrrolidinyl})\text{acetyl}$ ]-4-[ $(\text{trifluoromethyl})\text{phenyl}$ ]-  
(9CI) (CA INDEX NAME)



IT 150557-71-4P  
RL: BAC (Biological activity or effector, except adverse); SPN  
(Synthetic  
preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and antiviral activity of)  
RN 150557-71-4 CAPLUS  
CN Piperacline, 1-(2-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-  
(SCI)  
(CA INDEX NAME)

L14 ANSWER 157 OF 263 CAPSIS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1993-531752 CAPLUS  
DOCUMENT NUMBER: 1199-131752  
TITLE: Identification of residues important for ligand  
binding to the human 5-hydroxytryptamine1A  
serotonin receptor  
AUTHOR(S): Chanda, Pranab K.; Minchin, Michael C. W.;  
Davis, Alan R.; Greenberg, Lynda; Reilly, Yvonne; McGregor, William H.; Bhat, Ramesh; Lubeck, Michael D.;  
Hung, Paul P.  
CORPORATE SOURCE: Dep. Biotechnol. Microbiol., Wyeth-Ayerst Res.,  
Philadelphia, PA, 19101, USA  
SOURCE: Mol. Pharmacol. (1993), 43(4), 516-20  
DOCUMENT TYPE: CODEN: MOPMA3; ISSN: 0026-895X  
Journal  
LANGUAGE: English  
AB The functional significance of the conserved amino acids within  
transmembrane regions II and VII of the human 5-hydroxytryptamine  
(5-HT)1A  
receptor was analyzed by oligonucleotide-directed mutagenesis  
followed by  
transient expression of the mutated receptor genes in COS-1 cells.  
The substitution of a conserved asparagine at position 396 (transmembrane  
region VII) with either alanine, phenylalanine, or valine resulted  
in a receptor that did not bind the 5-HT1A agonist 8-hydroxy-2-(di-n-  
[3H]propylamino)tetralin. In contrast, replacement of Asn396 with  
glutamine did not affect agonist binding. In addn., serine residues  
at positions 391 and 393 (transmembrane domain VII) were changed to  
alanine. Changing the less conserved Ser391 to alanine had no effect on ligand  
binding. However, replacement of the conserved Ser393 with alanine  
reduced ligand binding by 86%. Replacement of a conserved aspartate  
at position 82 (transmembrane region II) with alanine also produced a  
receptor without detectable agonist binding. Protein immunoblotting  
detected receptor protein of approx. 51 kDa in both wild-type and  
mutant receptor-expressing cells, indicating that these mutations probably  
did not affect expression or processing of the protein. Importantly, the  
sequence of the human 5-HT1A receptor described in this paper  
differs from the published sequence in transmembrane region IV. The present  
sequence encodes a protein of 422 amino acids, instead of the 421-amino acid  
protein that has been described previously and has a change in the  
sequence in transmembrane region IV from...RPRAL... to...RRAAA...,  
which corresponds to the published sequence of the rat 5-HT1A receptor.  
Moreover, conversion of the transmembrane region IV sequence of the  
present clone to that of the published sequence by site-directed

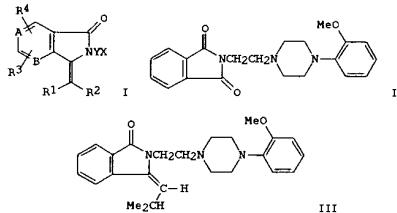
L14 ANSWER 157 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
11-azaspiro[5.5]-4-  
IT 21102-95-4  
RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); PRR (Properties); BIOL (Biological study,  
(5-HT1A receptor of human binding by, site for)  
RN 21102-95-4 CAPLUS  
CN 8-Azapiro[4.5]decan-7-9-dione, 8-[2-(4-methoxyphenyl)-1-piperazinyl]ethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HC

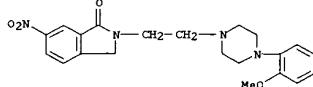
L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1993:495325 CAPLUS  
 DOCUMENT NUMBER: 119:95325  
 TITLE: Preparation of 3-methyleneisindolin-1-one derivatives  
 INVENTOR(S): Mohri, Shinichiro; Obase, Hircyuki; Ikeda, Junichi;  
 PATENT ASSIGNEE(S): Kubo, Kazuhiko; Mori, Akhisa; Ishii, Akio  
 SOURCE: Kyowa Hakko Kogyo Co., Ltd., Japan  
 PCT Int. Appl., 185 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9217448	A1	19921015	WO 1992-JP246	19920302
WI, CA, JP, US RW, AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE			JP 1991-68379	19910401
PRIORITY APPLN. INFO.: MARPAT 119:95325				
OTHER SOURCE(S): GI				

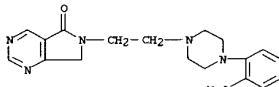


AB The title compds. [I; A, B = CH, N; R1, R2 = alkyl; R3, R4 = halo, alkoxy, etc.; X = (substituted) heterocycl; Y = (CH<sub>2</sub>)<sub>1-4</sub>] are prepnd. A soln. of Me<sub>2</sub>CH<sub>2</sub>MgBr in THF was added to a soln. of imide II in THF with stirring at room temp. under Ar, 4 N HCl was added with stirring, followed by H<sub>2</sub>O and 10 N NaOH, and the mixt. was extd. with EtOAc to give 50% III, which as a phosphate salt showed min. ED of 6.3 mg/kg p.o. for cerebral

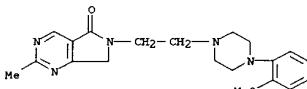
L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 protection in mice.  
 IT 149263-56-9P 149263-60-5P 149263-65-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 drug?  
 RN 149263-56-9 CAPLUS  
 CN 1H-Isindolin-1-one, 2,3-dihydro-2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl-6-nitro- (9CI) (CA INDEX NAME)



RN 149263-60-5 CAPLUS  
 CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

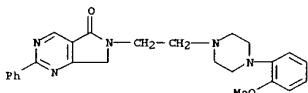


RN 149263-65-0 CAPLUS  
 CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)



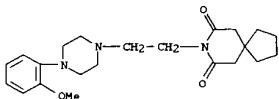
RN 149263-66-1 CAPLUS  
 CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-2-phenyl- (9CI) (CA INDEX NAME)

L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 159 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1993:421024 CAPLUS  
 DOCUMENT NUMBER: 119:21024  
 TITLE: Studies of the biochemical basis for the discriminative properties of 8-hydroxy-2-(di-n-propylamino)tetralin  
 AUTHOR(S): Raber, Richard A.; Winter, J. C.  
 CORPORATE SOURCE: Dep. Pharmacol., State Univ. New York, Buffalo, NY,  
 14214, USA  
 SOURCE: Eur. J. Pharmacol. (1993), 235(2-3), 237-43  
 CODEN: EUPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The ability of a series of compds. to mimic the stimulus properties of 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) was compared to: the affinity of these compds. for the 5-HT1A receptor; and their efficacy to inhibit forskolin-stimulated adenylate cyclase activity. Although for 8-OH-DPAT compds. (flexinoxan, MDL 73005EF, gepirone, ipsapirone, buspirone, tandospirone, yohimbine, L 657,743 and rawolscine) complete cross generalization was assocd. with high affinity for the 5-HT1A receptor, eltoprane, LSP and BMY 7378 had pK<sub>D</sub> > 7.44, but did not show complete mimicry of 8-OH-DPAT. In addn., indorenad had a pK<sub>D</sub> of 7.88, yet the behavioral response was indistinguishable from the saline control. Because the above data indicated that affinity for the 5-HT1A receptor was necessary, but not sufficient for a receptor ligand to mimic 8-OH-DPAT, the in vitro efficacy of the various compds. at the 5-HT1A receptor was detd. by measuring inhibition of forskolin-stimulated adenylate cyclase activity in hippocampal membranes. For a series of drugs (gepirone, ipsapirone, flexinoxan, buspirone, tandospirone, yohimbine, L 657,743 and rawolscine) inhibition of forskolin-stimulated adenylate cyclase activity was obsd., and these same drugs showed complete cross generalization. However, BMY 14802 and MDL 73005EF did not alter adenylate cyclase activity, yet completely mimicked the stimulus properties of 8-OH-DPAT. Eltoprane showed efficacy in inhibiting forskolin-stimulated adenylate cyclase activity, but only 30% of the responses following administration of this drug were on the 8-OH-DPAT-appropriate lever. Furthermore, although indorenad inhibited hippocampal adenylate cyclase activity, the behavioral response to this compd. was indistinguishable from the saline control. The present study indicates that activation of the 5-HT1A receptor neg. coupled to adenylate cyclase is neither necessary nor sufficient for a receptor ligand to mimic the stimulus properties of

L14 ANSWER 159 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 8-OH-DPAT.  
 IT 21102-95-4, BMY 7378  
 RL: 110-1 (Biological study)  
 (sigma receptor affinity of,  
 hydroxydipropylamine-tetralin  
 action in relation to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



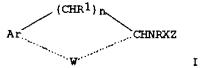
●2 HCl

L14 ANSWER 160 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1993:225698 CAPLUS  
 DOCUMENT NUMBER: 118:225698  
 TITLE: Preparation of .sigma. receptor ligands as drugs  
 for treatment of central nervous system disorders  
 INVENTOR(S): Glennon, Richard A.  
 PATENT ASSIGNEE(S): Virginia Commonwealth University, USA  
 SOURCE: PCT Int. Appl., 190 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9300313	A2	19930107	WO 1992-US5330	19920626
WO 9300313	A3	19930304		
W: AU, BE, BG, BR, CA, CS, FI, HU, JP, KP, KR, LX, MG, MN, MW, NO, PL, RO, RU, SD, RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 6057371	A	20000502	US 1992-894771	19920610
CA 2111957	AA	19930107	CA 1992-2111957	19920626
AU 9222945	A1	19930125	AU 1992-22945	19920626
AU 676993	B2	19970410		
ZA 9204775	A	19930416	ZA 1992-4775	19920626
EP 591426	A1	19940413	EP 1992-914789	19920626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE, JP 06509069	T2	19941013	JP 1992-561248	19920626
PRIORITY APPLN. INFO.: US 1991-720173			US 1991-720173	19910627
			US 1992-894771	19920610
			WO 1992-US5330	19920626

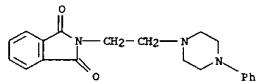
OTHER SOURCE(S): MARPAT 118:225698

GI



AB The phenylalkylamines, aminotetralins, piperazines, and piperidines I  
 [Ar] = (un)substituted aryl or heteroaryl; R = H, alkyl; R<sub>1</sub> = R, alkoxy, chloro, etc.; RR<sub>1</sub> = morpholino, piperazinyl, piperidinyl; V =  $(CH_2)_p$ , -H;  
 H; X =  $(CH_2)_q$ ,  $(CH_2)_rC.tpbond.(CH_2)_s$ , etc.; Z = H, cycloalkyl, aryl, etc.; n = 0-5; p = 1-3; q = 1-6; r = 0-3] are prep'd. as selective .sigma.-receptor-binding agents, useful for the treatment of gastroenteral

L14 ANSWER 160 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 bind to dopaminergic, PCP and 5-HT1A receptors, they are free of the side effects of the conventional neuroleptic agents. The reaction of R-(+)-amphetamine with 2-phenoxyethyl chloride, at 95.degree., gave R-(+)-N-(2-phenoxyethyl)-1-phenyl-2-aminopropane-HCl. The .sigma.-, PCP-, and dopamine-receptor binding assays were carried out by the method of Weber et al. (1986), using guinea pig brain membrane homogenates and the radioligand [<sup>3</sup>H]di-o-tolylguanidine.  
 IT 75000-24-7  
 RL: BIOL (Biological study)  
 (central nervous and gastrointestinal agent, as sigma receptor ligand)  
 RN 75000-24-7 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 161 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1993:94851 CAPLUS  
 DOCUMENT NUMBER: 118:94851  
 TITLE: Allosteric interactions between the binding sites

of receptor agonists and guanine nucleotides: A comparative study of the 5-hydroxytryptamineA and adenosine A<sub>1</sub> receptor systems in rat hippocampal membranes

Mahle, Cathy D.; Wiener, Harvey L.; Yucca, Frank D.; Maayani, Saul

CORPORATE SOURCE: Mount Sinai Sch. Med., City Univ. New York, New York,

SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(3), 1275-84  
 CODEN: JPEAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The ternary complex formed between agonist, receptor, and guanine nucleotide-binding protein and its destabilization by guanine nucleotides

(GN) were utilized to study early events in signal transduction, by characterizing the allosteric interactions between agonist and GN binding to the receptor/guanine nucleotide-binding protein, G complex for adenosine A<sub>1</sub> and 5-HT1A receptors. The functional interaction between the ternary complex and GTP was examed. by assaying adenylyl cyclase activity.

Binding of a full adenosine A<sub>1</sub> agonist ([<sup>3</sup>H]-R-(+)-N<sub>6</sub>-(2-phenoxypropyl)adenosine) and a full ( $+/-$ )-[<sup>3</sup>H]-8-hydroxydipropylamino-tetralin ([<sup>3</sup>H]I) and partial ([<sup>3</sup>H]-8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiron[4.5]-decan-7,9-dione) ([<sup>3</sup>H]II) 5-HT1A agonist was examed. in relation to the binding of GN.

The amt. of ternary complex formed depended upon receptor type and drug relative efficacy. The ratio between the drug's EC<sub>50</sub> value (adenylyl cyclase) and dissoch. const. (K<sub>d</sub>) was also receptor and drug relative efficacy dependent. 5'-Guanylylimidodiphosphate (100 .mu.M) caused an apprx. 50% decrease in the Bmax for all drugs without affecting K<sub>d</sub> values.

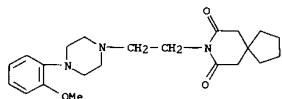
5'-Guanylylimidodiphosphate and guanosine 5'-O-(3-thiotriphosphate) attenuated [<sup>3</sup>H]-agonist binding in a concn.-dependent and saturable manner, with IC<sub>50</sub> values increased 2-6-fold with increasing receptor occupancy. IC<sub>50</sub> values were approx. one-tenth lower at the 5-HT1A receptor than at the adenosine A<sub>1</sub> receptor; similar values were obtained

for inhibition of [<sup>3</sup>H]I and [<sup>3</sup>H]II binding, suggesting an independence of agonist efficacy. It is proposed that the stabilization of the ternary complex by hormone binding, measured by Bmax values, is related to drug-relative efficacy; thus, the amt. of ternary complex available for destabilization by GN is greater for the more efficacious agonist. This

L14 ANSWER 161 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 is translated into greater relative efficacy obmd. in the maximal inhibition of adenylyl cyclase.

IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (serotonergic S1A receptor binding of, in hippocampus,  
 allosteric interactions between binding sites of receptor agonist and guanine nucleotides in relation to)

RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

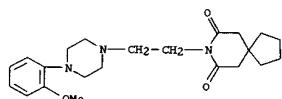
L14 ANSWER 162 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESION NUMBER: 1993:32850 CAPLUS  
 DOCUMENT NUMBER: 118:32850  
 TITLE: Yohimbine as a serotonergic agent: evidence from receptor binding and drug discrimination

AUTHOR(S): Winter, J. C.; Rabin, Richard A.  
 CORPORATE SOURCE: Sch. Med. Biomed. Sci., State Univ. New York, Buffalo, NY, USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(2), 682-9  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Stimulus control was established in rats trained to discriminate either 8-hydroxy-2-(di-n-propylamino)tetralin (DPAT) (0.2 mg/kg or yohimbine (3 mg/kg) from saline. Tests of generalization were then conducted with a group of drugs thought to act via the 5-hydroxytryptamine1A (5-HT1A) receptor and a group to drugs thought to act as antagonists at .alpha.2-adrenoceptors. In addn., each drug was characterized in terms of its affinity for 5-HT1A and .alpha.2-adrenoceptors by means of radioligand binding techniques. It was obmd. that the stimulus effects of DPAT generalized fully to those of the .alpha.2-adrenoceptor antagonists, yohimbine, rauwolscine and L-657,743, but not to idazoxan or atipamezole. In addition, consts. (Kd, nM) of the .alpha.2-adrenoceptor antagonists at the 5-HT1A receptor were 74, 52, 80, 199 and 13,000, resp. Thus, the discrimination data are explicable in terms of a direct action of yohimbine and some other .alpha.2-adrenoceptor antagonist upon 5-HT1A receptors. In yohimbine-trained rats, full generalization to DPAT, flesinoxan and tandospirone was obmd. In light of the negligible affinity of flesinoxan and tandospirone for the .alpha.2-adrenoceptor (9000 and 8800 nM, resp.), and high affinity for the 5-HT1A receptor (0.3 and 43 nM, resp.), a mechanism mediated by the latter site is suggested. The present data suggest that rats trained with yohimbine as a discriminative stimulus generalize to drugs with minimal affinity for the .alpha.2-adrenoceptor but with high affinity for 5-HT1A receptors. Studies in which yohimbine is used to assess the function of the .alpha.2-adrenoceptor should also consider the possible involvement of 5-HT1A receptors.

IT 21102-95-4, BMY7378  
 RL: BIOL (Biological study)  
 (yohimbine binding to serotonergic S1A and .alpha.2-adrenergic receptors response to)

RN 21102-95-4 CAPLUS

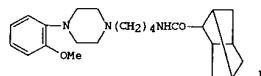
L14 ANSWER 162 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

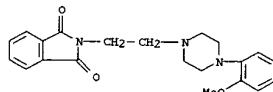
L14 ANSWER 163 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESION NUMBER: 1992:626102 CAPLUS  
 DOCUMENT NUMBER: 117:626102  
 TITLE: 4-[4-(1-Noradmantane-carboxamide)butyl]-1-(2-methoxyphenyl)piperazine: a high-affinity 5-HT1A-selective agent

AUTHOR(S): Stacy El-Bermawy, Mohamed; Raghupathi, Reva; Ingher, P.; Teitler, Milt; Maayani, Saul; Glennon, Richard A.  
 CORPORATE SOURCE: Dep. Med. Chem., Med. Coll. Virginia, Richmond, VA, USA  
 SOURCE: Med. Chem. Res. (1992), 2(2), 88-95  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

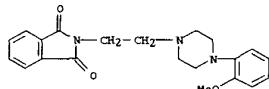


AB A problem with many arylpiperazine 5-HT1A ligands is their high affinity for .alpha.1-adrenergic, D2 dopamine, and/or 5-HT2 serotonin receptors. The title compd. (I) binds with very high affinity at 5-HT1A receptors (Ki = 0.1 nM) and with 460- 260- and 400-fold selectivity over .alpha.1-adrenergic, D2, and 5-HT2 receptors, resp. Preliminary studies indicate that I is a 5-HT1A partial agonist (intrinsic activity = 0.4) with 140-fold the affinity of the std. agent buspirone.

IT 99718-67-9P 144291-58-5  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as high affinity 5-HT1A-selective agent)  
 RN 99718-67-9 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

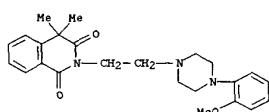


RN 144391-85-5 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-  
 , monohydrochloride (9CI) (CA INDEX NAME)



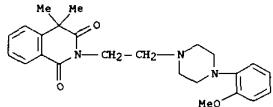
● HCl

L14 ANSWER 164 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:605626 CAPLUS  
 DOCUMENT NUMBER: 117:205626  
 TITLE: The .alpha.2-adrenoceptors of the human  
 retinoblastoma  
 example of cell line (Y79) may represent an additional  
 AUTHOR(S): Gleason, Marie M.; Hieble, J. Paul  
 CORPORATE SOURCE: Dep. Pharmacol., SmithKline Beecham Pharm., King  
 of Prussia, PA, 19406, USA  
 SOURCE: Br. J. Pharmacol. (1992), 107(1), 222-5  
 CODEN: BJPCM; ISSN: 0007-1189  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In agreement with the literature, correlation of the ability of a series of agonists and antagonists to displace [<sup>3</sup>H]rauwolscine binding shows the alpha.2-adrenoceptors of HT29 cells, NG108-15 cells, OK cells, and homogenates of rat sublingual gland to represent 4 distinct subtypes. [<sup>3</sup>H]rauwolscine also bound with high affinity ( $K_D = 0.30 \text{ nM}$ ) to a human retinoblastoma cell line (Y79). Specific binding represents 73% of total binding, and a  $B_{max}$  of 38 fmol/mg protein was detd. Correlation of antagonist affinities against [<sup>3</sup>H]rauwolscine with corresponding values in the other 4 tissue sources showed the Y79 cells to resemble most closely the OK cells, the prototype example of an .alpha.2C-adrenoceptor, with a correlation coeff. of 0.90 and a regression slope of 1.01 being obtained for 10 antagonists in these two systems. Comparison of  $K_D$  values for [<sup>3</sup>H]rauwolscine also showed a similarity between the OK cells (0.19 nM) and Y79 cells. These data suggest that the human retinoblastoma cell line may represent an addnl. example of the .alpha.2C-adrenoceptor subtype.  
 IT 67339-62-2 ANC-239  
 RI: BIOC (Biological study)  
 (rauwolscine binding by various .alpha.2-adrenoceptor subtypes inhibition by)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinodiones, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



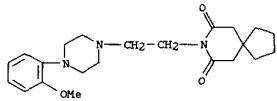
L14 ANSWER 165 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:543163 CAPLUS  
 DOCUMENT NUMBER: 117:143163  
 TITLE: .alpha.2 Adrenoceptor and catecholamine-insensitive binding sites for [<sup>3</sup>H]rilmendine in membranes from rat cerebral cortex  
 AUTHOR(S): King, Paul R.; Gundlach, Andrew L.; Jarrott, Bevyn; Louis, William J.  
 CORPORATE SOURCE: Clin. Pharmacol. Ther. Unit, Austin Hosp., Heidelberg, 3084, Australia  
 SOURCE: Eur. J. Pharmacol. (1992), 218(1), 101-8  
 CODEN: EJPMAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The kinetic and pharmacol. characteristics of the binding of the oxazoline antihypertensive drug, [<sup>3</sup>H]rilmendine, to membranes of rat cerebral cortex have been detd. Computerized resoln. of curvilinear, equil. binding isotherms was consistent with the existence of two distinct binding sites for [<sup>3</sup>H]rilmendine:  $K_D$  17.3 .+- .7.41 nM,  $B_{max}$  0.197 .+- .0.06 pmol/mg protein and  $K_D$  254 .+- .48 nM,  $B_{max}$  1.59 .+- .0.08 pmol/mg protein. Moreover, the resoln. of two assocn. and dissoch. rates also suggested the existence of two binding site populations. Drug inhibition studies revealed that specific binding of [<sup>3</sup>H]rilmendine (2 nM) was only inhibited by a max. of 50% by the catecholamines, adrenaline and noradrenaline, but was completely inhibited by some oxazolines, by guanabenz (a guanidino drug) and by several imidazoline compds. including neprazoline, oxymetazoline and clonidine. Binding isotherms for these drugs were also best fit by a two-site model. The relative  $K_I$  values at the high affinity site for [<sup>3</sup>H]rilmendine and the no. of these high affinity sites are consistent with this site being an .alpha.2-adrenoceptor. The high affinity of oxymetazoline and low affinity of prazosin for high affinity [<sup>3</sup>H]rilmendine binding sites together with rank order of potency of oxymetazoline > phentolamine > SKF 104078 > ANC-239 > prazosin suggest that [<sup>3</sup>H]rilmendine binds to the .alpha.2A sub-type of adrenoceptor. Computer-resolved  $K_I$  values for drugs at the larger no. of lower affinity binding sites were very similar to  $K_I$  values detd. in the presence of 10 .mu.M adrenaline (used to block .alpha.2-adrenoceptor binding). The catecholamine-insensitive binding site did not share the pharmacol. characteristics of previously described, high affinity imidazoline-guanidinium receptive sites or high affinity imidazoles sites, but more closely resembles the so-called "idszoxan receptor".

L14 ANSWER 165 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
IT 67339-62-2, ARK-239  
RL: PRP (Properties)  
(affinity of, for rilmenidine binding sites in cerebral cortex)  
RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (SC1) (CA INDEX NAME)



L14 ANSWER 166 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1992:524363 CAPLUS  
DOCUMENT NUMBER: 117:124363  
TITLE: Discriminative stimulus effects of 8-OH-DPAT in pigeons: antagonism studies with the putative 5-HT1A receptor antagonists BMY 7378 and NAN-190  
AUTHOR(S): Barrett, James E.; Gleeson, Suzanne  
CORPORATE SOURCE: Med. Res. Div., American Cyanamid Co., Pearl River, NY, 10565, USA  
SOURCE: Eur. J. Pharmacol. (1992), 217(2-3), 163-71  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Pigeons were trained to discriminate 0.3 mg/kg of the 5-HT1A receptor agonist 8-hydroxy-2-(di-N-propylamino)tetralin (8-OH-DPAT) from saline. RU 24969 (5-methoxy-3-(1,2,3,6-tetrahydrcypridin-4-yl)-1H-indole), at doses of 5.6-10 mg/kg, and eltoprazine (5.6 mg/kg), both mixed 5-HT1A/B agonists, substituted completely for 8-OH-DPAT, whereas 3.0-10 mg/kg of the 5-HT 1B/C agonist TFMPP (1-(n-trifluoromethylphenyl)piperazine) and 0.1-3.0 of the 5-HT3 antagonist MDL 72222 (3-tropanyl-3,5-dichlorobenzoate) yielded only saline-appropriate responses. Substitution for 8-OH-DPAT by eltoprazine and RU 24969, which does not occur in rats, provides in vivo support for the suggestion that the absence of a 5-HT1B receptor in the pigeon allows more complete expression of 5-HT1A-mediated effects. BMY 7378 (8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]8-azaspiro-[4.5]-decane-7,9-dione) attenuated the 8-OH-DPAT stimulus at doses from 1.0 to 10 mg/kg but, when administered alone, also resulted in approx. 40% 8-OH-DPAT-appropriate responding at the highest dose. NAN-190 (1-(2-methoxyphenyl)-4-[4-(2-phthalamido)butyl]-piperazine (0.3-3.0 mg/kg) produced a dose-dependent and complete antagonism of the 8-OH-DPAT-discriminative stimulus; administered alone NAN-190 resulted only in saline-key responding. NAN-190 also reversed the rate-reversing effects of higher doses of 8-OH-DPAT. The beta-adrenoceptor antagonist (+)-pindolol (5.6-17 mg/kg) antagonized the discriminative stimulus effects of lower 8-OH-DPAT doses but was unable to block the effects of higher doses of 8-OH-DPAT. Frazosin (1.0-10 mg/kg), which like NAN-190, is an alpha-1-antagonist, neither substituted for nor blocked the discriminative stimulus effects of 8-OH-DPAT. These results suggest that NAN-190 is an effective 5-HT1A receptor antagonist in this procedure with

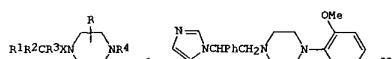
L14 ANSWER 166 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
pigeons with no indication of agonist actions, whereas BMY 7378 and pindolol are best characterized as partial 5-HT1A receptor agonists.  
IT 21102-95-4, BMY 7378  
RL: BIOL (Biological study)  
(serotonergic 5IA partial agonism by, in pigeons)  
RN 21102-95-4 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (SC1) (CA INDEX NAME)



•2 HCl

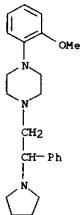
L14 ANSWER 167 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1992:490321 CAPLUS  
DOCUMENT NUMBER: 117:09321  
TITLE: Piperazine derivatives  
INVENTOR(S): Ward, Terence James; Warrelton, Graham John  
PATENT ASSIGNEE(S): John Wyeth and Brother Ltd., UK  
SOURCE: Eur. Pat. Appl., 16 pp.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	XIND	DATE	APPLICATION NO.	DATE
EP 479546	A2	19920408	EP 1991-308969	19911001
EP 479546	A3	19920603		
EP 479546	B1	19961030		
R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE AU 9184883	A1	19920409	AU 1991-84883	19910930
AU 642532	B2	19931021		
US 5177078	A	19930105	US 1991-768147	19910930
GE 2248616	A1	19920415	GB 1991-20856	19911001
GE 2248616	B2	19930415		
JP 0557570	A2	19920911	JP 1991-253585	19911001
AT 144772	E	19961115	AT 1991-308969	19911001
ES 2094204	T3	19970116	ES 1991-308969	19911001
CA 2052619	AA	19920404	CA 1991-2052619	19911002
HU 59394	A2	19920528	HU 1991-3160	19911003
HU 217813	B	20000428		
IL 101166	A1	20000813	IL 1992-101166	19920306
PRIORITY APPLN. INFO.:			GB 1990-21453	A 19901003
OTHER SOURCE(S):			MARPAT 117:90321	
GI				

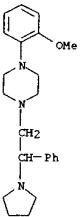


AB = Piperazines I (X = alkylene; R = H, alkyl; R1, R4 = aryl, heteroaryl, mono- or bicyclic heterocyclic; R3 = H, OH, alkyl) were prepd. Thus, 1-(2-methoxyphenyl)piperazine was treated with styrene oxide followed by imidazole to give the piperazine II. II had 5-hydroxytryptamine type 1A receptor antagonist activity in rats at a min. ED of 1 mg/kg s.c. and 10 mg/kg orally.  
IT 141733-67-7P 142234-29-5P  
RL: SFN (Synthetic preparation); PREP (Preparation) (prepn. of)

L14 ANSWER 167 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 141733-67-7 CAPLUS  
 CN Piperazine, 1-(2-methoxyphenyl)-4-[2-phenyl-2-(1-pyrrolidinyl)ethyl]-  
 (9CI) (CA INDEX NAME)



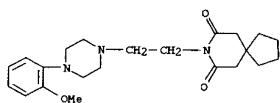
RN 142234-29-5 CAPLUS  
 CN Piperazine,  
 1-(2-methoxyphenyl)-4-[2-phenyl-2-(1-pyrrolidinyl)ethyl]-  
 dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

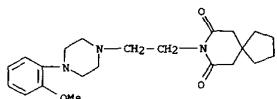
L14 ANSWER 168 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:483356 CAPLUS  
 DOCUMENT NUMBER: 117:83356  
 TITLE: Evidence for postsynaptic mediation of the  
 hypothermic effect of 5-HT1A receptor activation  
 AUTHOR(S): O'Connell, M. T.; Sarna, G. S.; Curzon, G.  
 CORPORATE SOURCE: Dep. Neurochem., Inst. Neurol., London, WC1N 3BG,  
 UK  
 SOURCE: Br. J. Pharmacol. (1992), 106(3), 603-9  
 CODEN: BJPCBM; ISSN: 0007-1188  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The 5-HT1A ligand BMY 7378 (8-[2-(2-methoxyphenyl)-1-piperazinyl]ethyl)-8-  
 azaspiro [4.5]-decane-7,9-dione dihydrochloride, 0.032-2 mg kg-1,  
 s.c.) caused hyperphagia, a response to the activation of presynaptic 5-HT1A  
 receptors. BMY 7378 (8 mg kg-1, s.c.) and the 5-HT1A agonist  
 (8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT), 0.10 and 0.25 mg  
 kg-1, s.c.) also caused hypothermia. This was inhibited by  
 (-)-pinoclocol (1  
 mg kg-1, i.p.) and not prevented by pretreatments with  
 p-chlorophenylalanine which grossly depleted 5-hydroxytryptamine  
 (5-HT) from terminal regions. The hypothermic effects are explicable by  
 activation of postsynaptic 5-HT1A receptors. Infusion of BMY 7378  
 (8-64  
 .mu.g) into the dorsal raphe was without convincing hypothermic  
 effect.  
 BMY 7378 (8 mg kg-1, s.c.) inhibited another effect of activation of  
 postsynaptic 5-HT1A receptors, i.e., the induction of components of  
 the 5-HT syndrome by 8-OH-DPAT (0.5, 1.0 mg kg-1, s.c.) which suggests  
 that BMY 7378 has antagonistic as well as agonistic effects at these sites.  
 Partial agonist properties of BMY 7378 at postsynaptic sites were also  
 indicated by doses for hypothermia being much greater than those for  
 hyperphagia i.e., ED50 (hypothermia)>2 mg kg-1, ED50 (hyperphagia)=  
 0.010  
 mg kg-1. This contrasts with the similar ED50 values for both the  
 hypothermic (ED50 = 0.08-0.10 mg kg-1) and hyperphagic (ED50 =  
 0.06-0.10  
 mg kg-1) effects of 8-OH-DPAT. The evidence obtained for mediation  
 of the hypothermic response to 5-HT1A agonists by postsynaptic sites is  
 relevant  
 to the interpretation of the effect on it of antidepressant  
 treatments and  
 depressive illness.  
 IT 21102-95-4, BMY 7378  
 RL: PRP (Properties)  
 (hypothemic and hyperphagic and behavioral effects of,  
 serotonergic  
 SIA receptors in relation to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspido[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 168 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 169 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:420443 CAPLUS  
 DOCUMENT NUMBER: 117:20443  
 TITLE: The putative 5-HT1A antagonist BMY 7378 blocks  
 8-OH-DPAT-induced changes in local cerebral  
 glucose utilization in the conscious rat  
 AUTHOR(S): Grahame-Smith, D.  
 CORPORATE SOURCE: Univ. Dep. Clin. Pharmacol., Radcliffe Infir.,  
 Oxford, OX2 6HE, UK  
 SOURCE: Neuropharmacology (1992), 31(6), 547-51  
 CODEN: NEPHEW; ISSN: 0028-3908  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB It has previously been shown that the 5-HT1A agonist, 8-OH-DPAT,  
 caused  
 discrete changes in cerebral glucose utilization in the rat, as  
 assessed  
 by quant. 2-deoxyglucose autoradiog. Here, the effect of the putative  
 5-HT1A antagonist, BMY 7378, on regional cerebral glucose utilization  
 was  
 examed., when injected alone and in rats treated with 8-OH-DPAT. In  
 control rats, BMY 7378 (5 mg/kg, s.c.) markedly increased glucose  
 utilization in the lateral habenular nucleus and moderately reduced  
 glucose utilization in the hippocampal formation. Pretreatment with  
 BMY  
 7378 (5 mg/kg) significantly attenuated the redns. in glucose  
 utilization  
 in the hippocampus, entorhinal, piriform and cingulate cortex,  
 induced by  
 8-OH-DPAT (0.25 mg/kg). The 8-OH-DPAT-induced increase in glucose  
 utilization in the copula pyramidis, that is putatively assoc. with the  
 appearance of the 5-HT behavioral syndrome, was also blocked by BMY  
 7378,  
 as was the behavioral syndrome. In summary, BMY 7378 produced few of  
 the  
 discrete changes in cerebral glucose utilization that are seen with  
 8-OH-DPAT. However, many of the changes induced by 8-OH-DPAT were  
 reversed by BMY 7378. These data are consistent with the hypothesis  
 that  
 the effects of 8-OH-DPAT on regional cerebral glucose utilization are  
 mediated by 5-HT1A receptors.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (8-OH-DPAT-induced brain regional glucose utilization blockade by,  
 serotonin SIA receptors in)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspido[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-



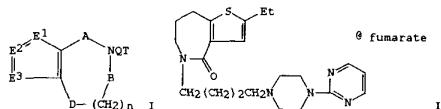
●2 HCl

L14 ANSWER 170 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:194290 CAPLUS  
 DOCUMENT NUMBER: 116:194290  
 TITLE: Preparation of thienoazepinone compounds and  
 their use  
 INVENTOR(S): Nakao, Tohru; Tanaka, Hiroshi; Yamato, Hirotake;  
 Akagi, Takeshi; Takehara, Shuzo  
 PATENT ASSIGNEE(S): Yushitomo Pharmaceutical Industries, Ltd., Japan  
 SOURCE: Eur. Pat. Appl., 74 pp.  
 CODEN: EPXXW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 465254	A1	19920108	EP 1991-306095	19910704
EP 465254	B1	19921113		
AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 05043592	A2	19930223	JP 1991-191087	19910704
AT 145208	E	19961115	AT 1991-306095	19910704
CA 2046368	AA	19920107	CA 1991-2046368	19910705
US 5141930	A	19920825	US 1991-726683	19910705
PRIORITY APPLN. INFO.:				
			JP 1990-179953	19900706
			JP 1990-232244	19900831
			JP 1990-326644	19901127
			JP 1991-13684	19910111
			JP 1991-75657	19910314

OTHER SOURCE(S): MARPAT 116:194290

GI



AB Title compds. I (one of E1, E2, E3 is S and the other 2 are R1C, R2C wherein R1, R2 = H, halo, O2N, H2N, cyano, HO, CHO, alkyl, alkoxy, haloalkyl, (substituted) H2NSO2, alkylthio, HO2C, etc.; D = CH2, S(O)m wherein m = 0-2; Q = alkylene; T = amino, heterocyclyl; A = CO, CS, CH2; B = CO, CS) or a salt thereof, useful as antianxietics, antipsychotics and

for treatment of circulatory disorders, are prep'd.

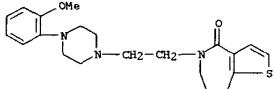
2-Acetyl-5-[4-(4-

pyrimidinyl)-1-piperazinyl]butyl-5,6,7,8-tetrahydro-4H-thieno[3,2-c]azepin-4-one (prepn. given) in F3CCO2H was added Et3SiH, the mixt. stirred for 20

L14 ANSWER 170 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 h at room temp to give after work-up and addn. of fumonic acid the thienoazepinone II. In the receptor binding test, the Ki (nM) of II for 5-HT1A, 5-HT2, and D2 was 1.3, 990.0 and 78.0, resp., and the anxiolytic effect was (min. ED) 1.0 mg/kg, p.o. Addn. I were prep'd. and tested. A tablet formulation comprising I is given.

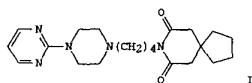
IT 140217-04-5P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthesis); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (prepn. of, as drug)

RN 140217-04-5 CAPLUS  
 CN 4H-Thieno[3,2-c]azepin-4-one,  
 5,6,7,8-tetrahydro-5-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

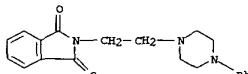
L14 ANSWER 171 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:193385 CAPLUS  
 DOCUMENT NUMBER: 116:193385  
 TITLE: Unexpected configuration of molecules of buspirone and its analogs in solution  
 AUTHOR(S): Bondarev, M. L.; Kalyuskii, A. R.; Shapiro, Yu. E.; Andronati, S. A.  
 CORPORATE SOURCE: Fiz.-Khim. Inst., Odessa, USSR  
 SOURCE: Ukr. Khim. Zh. (Russ. Ed.) (1991), 57(9), 986-91  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 GI



AB NMR results for buspirone (I) and several analogs in CD2Cl2, including spin-lattice relaxation times and Overhauser effects, indicated that a nearly chelate structure was preferred, possibly because of dipole-dipole interaction.

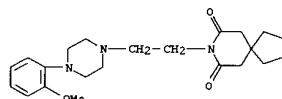
IT 75000-24-7  
 RL: PRP (Properties)  
 (conformation of, NMR in relation to)

RN 75000-24-7 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 172 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:143745 CAPLUS  
 DOCUMENT NUMBER: 116:143745  
 TITLE: Antagonism studies with BMY-7378 and NAN-190:  
 effects  
 AUTHOR(S): Ahlers, Stephen T.; Weissman, Ben Avi; Barrett,  
 James  
 E.  
 CORPORATE SOURCE: Neurochem. Div., Nav. Med. Res. Inst., Bethesda,  
 MD,  
 USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1992), 260(2), 474-81  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The purported serotonin (5-HT)1A antagonists BMY-7378 and NAN-190  
 were examined in pigeons for their potential to block the effects of the  
 prototypical 5-HT1A agonist 8-OH-DPAT on punished ("conflict") and  
 unpunished behavior and for their binding affinity at the 5-HT1A  
 receptor site labeled by [3H]-8-OH-DPAT. Although BMY-7378 and NAN-190 both  
 displayed high affinity for the 5-HT1A receptor (IC<sub>50</sub> values of 0.8  
 and 7.5 nM, resp.), their effects, when administered alone, as well as in  
 combination with 8-OH-DPAT, were distinct. 8-OH-DPAT (0.3-3.0 mg/kg)  
 produced large increases in punished responding at doses that did not  
 affect or that decreased unpunished responding. Administration of  
 NAN-190 (1.0-3.0 mg/kg) did not increase punished responding, whereas  
 BMY-7378 (1.0-5.6 mg/kg) slightly increased behavior suppressed by punishment.  
 Pretreatment with BMY-7378 attenuated the rate-increasing effects of  
 8-OH-DPAT on punished responding; however, these effects were  
 accompanied by dose-dependent enhancement of the rate-decreasing effects of  
 8-OH-DPAT  
 on unpunished responding. In contrast, NAN-190 blocked the  
 rate-increasing effects of 8-OH-DPAT on punished responding and also  
 reversed the rate-decreasing effects of 8-OH-DPAT on responding that  
 was not punished. Pretreatment with NAN-190 failed to block increases in  
 punished responding produced by 0.1 to 1.9 mg/kg of the  
 benzodiazepine midazolam. These data suggest that NAN-190 may be characterized as  
 an antagonist and BMY-7378 a partial agonist with respect to  
 5-HT1A-induced behavioral changes observed in the conflict procedure with pigeons.  
 IT 21102-95-4, BMY-7378  
 RL: BIOL (Biological study)  
 brain (serotonergic S1A receptor binding by, as partial agonist, in  
 cerebrum, conflict behavior response to)  
 RN 21102-95-4 CAPLUS

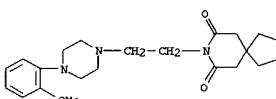
L14 ANSWER 172 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 173 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:143743 CAPLUS  
 DOCUMENT NUMBER: 116:143743  
 TITLE: The putative 5-HT1A receptor antagonists NAN-190  
 and BMY 7378 are partial agonists in the rat dorsal  
 raphe nucleus in vitro  
 AUTHOR(S): Greuel, Joachim M.; Glaser, Thomas  
 CORPORATE SOURCE: Inst. Neurobiol., Troponwerke G.m.b.H. und Co.  
 K.-G., Cologne, D-5000/80, Germany  
 SOURCE: Eur. J. Pharmacol. (1992), 211(2), 211-19  
 CODEN: EUPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal Article  
 LANGUAGE: English  
 AB The present electrophysiological study examined the actions of the putative  
 5-HT1A receptor antagonists, NAN-190 (1-(2-methoxyphenyl)-4-[4-(2-phthalimidobutyl)piperazine-HBr]) and BMY 7378  
 (8-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-8-azaspiro[4.5]dione-7,9-dione-2HCl) in the rat  
 dorsal raphe nucleus in vitro. There was no major difference  
 between the  
 effects of the two drugs on any measure investigated. Both compds.  
 reduced neuronal activity in a concn.-dependent manner, with BMY 7378  
 being slightly more potent than NAN-190. The threshold concns.  
 eliciting  
 inhibitory effects were 1 nM for BMY 7378 and 3 nM for NAN-190.  
 Complete  
 inhibition occurred at concns. close to 30 nM. The effects of the  
 5-HT1A  
 receptor agonist 8-OH-DPAT (8-hydroxy-2-(dipropylamino)tetralin)  
 could be  
 antagonized when concns. of NAN-190 or BMY 7378 were used that were  
 too low to produce a marked inhibition. At concn. close to threshold  
 both  
 compds. potentiated the inhibitory effects of 3 nM 8-OH-DPAT. The  
 suppression of neuronal firing induced by NAN-190 and BMY 7378 could  
 be completely antagonized with propranolol, indicating that the  
 inhibitory  
 actions of both drugs were not primarily due to alpha 1-adrenoceptor  
 antagonism. By applying theorems of receptor theory, the intrinsic  
 activities for both NAN-190 and BMY 7378 were calcd. to be in the  
 range of  
 0.1-0.3. Thus, NAN-190 and BMY 7378 are partial agonists in the rat  
 dorsal raphe nucleus. The results can be best explained by assuming  
 that  
 a crit. threshold of receptor occupancy has to be reached in order to  
 elicit a biol. response and by assuming a receptor reserve that may  
 account for the apparent full agonism of NAN-190 and BMY 7378.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (serotonergic S1A antagonistic and partial agonistic activity  
 of, in brain dorsal raphe nucleus)

L14 ANSWER 173 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

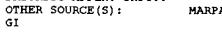


●2 HCl

L14 ANSWER 174 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:41481 CAPLUS  
 DOCUMENT NUMBER: 116:41481  
 TITLE: Preparation of new piperazine- and  
 piperidine-containing  
 azaspiro[4.5]decane-7,9-dione derivatives with serotoninergic activity  
 INVENTOR(S): Orjales Venero, Aurelio; Rodes Solanes, Rosa  
 PATENT ASSIGNEE(S): Fábrica Española de Productos Químicos y  
 Farmaceuticos  
 S. A. (PFAES), Spain

SOURCE: Spain, 8 pp.  
 CODEN: SPXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Spanish  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

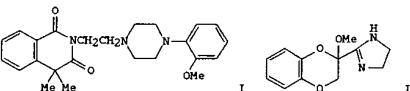
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2019228	A6	19910601	ES 1990-421	19900213
FI 9100652	A	19910814	FI 1991-652	19910211
EP 447345	A2	19910918	EP 1991-500014	19910211
EP 447345	A3	19920415		
R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, NL, SE NO 9100564	A	19910814	NO 1991-564	19910212
AU 9170983	A1	19910815	AU 1991-70983	19910212
CA 2036269	AA	19910814	CA 1991-2036269	19910213
JP 0809221	A2	19960409	JP 1991-41144	19910213
PRIORITY APPLN. INFO.: ES 1990-421				19900213
OTHER SOURCE(S): MARPAT 116:41481				GI



I

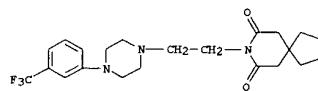
AB Title compds. I [X = N, CH; n = 2 or 4; Z = pyrimidin-2-ylamino, 3-F3CC6H4, or benzimidazol-2-yl substituted in 1-position by lower alkyl] or 4-FC6H4CH2] are prep'd. by cyclocondensation of 3,3-tetramethylene glutaric anhydride (II) with corresponding amines in, e.g., pyridine, PhMe, or BuOH, at 80-140.degree., preferably at reflux temp. Thus, reaction of II with 1-(4-aminobutyl)-4-[3-(trifluoromethyl)phenyl]piperazine in refluxing pyridine over 20 h gave 66% I (X = N, n = 4, Z = 3-F3CC6H4). I showed 5-HT1A receptor activity (displacement of [3H]-8-OH-DPAT from rat frontal cortex tissue) similar to

L14 ANSWER 175 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:671300 CAPLUS  
 DOCUMENT NUMBER: 115:271300  
 TITLE: Delineation of three pharmacological subtypes of .alpha.2-adrenoceptors in the rat kidney  
 AUTHOR(S): Uhlen-Staffan; Wikberg, Jarl E. S.  
 CORPORATE SOURCE: Dep. Pharmacol., Umeå University, Umeå, S-901 87, Sweden.  
 SOURCE: Br. J. Pharmacol. (1991), 104(3), 657-64  
 CODEN: BJPCBM; ISSN: 0007-1188  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

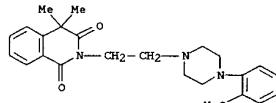


AB Simultaneous computer modeling of plain and ARC 239 (I)- and guanoxabenz-masked [3H]-RX 621002 (II) satn. curves, plain I and guanoxabenz competition curves as well as I-masked guanoxabenz competition curves revealed that the drugs bound to three .alpha.2-adrenoceptor subtypes in the rat kidney with grossly differing selectivities. These .alpha.2-adrenoceptor subtypes were termed .alpha.2A, .alpha.2B1, and .alpha.2B2. The order of affinities for [3H]II for the adrenoceptor sites was .alpha.2A > .alpha.2B1 > .alpha.2B2, the Kds being 0.62, 2.25, and 6.74 nM, resp. The order of affinities for I was .alpha.2B1 > .alpha.2B2 > .alpha.2A with Kds 4.78, 28.8, and 1460 nM, resp. For guanoxabenz the order of affinities was .alpha.2A > .alpha.2B1 > .alpha.2B2 with Kds 99.7, 508, and 25,400 nM, resp. The affinities of guanoxabenz for .alpha.2B1- and .alpha.2B2-adrenoceptors differed 72-fold and for .alpha.2A- and .alpha.2B2-adrenoceptors 380-fold. The selectivities of a no. of other drugs were less marked but their Kds were consistent with all 3 sites being .alpha.2-adrenoceptors. (-)-Adrenaline and (-)-noradrenaline showed dissimilar order of affinities for the three .alpha.2-adrenoceptors. For (-)-adrenaline the order of affinities was .alpha.2B1 > .alpha.2A > .alpha.2B2 and for (-)-noradrenaline

L14 ANSWER 174 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 buspirone (Ki = 1.99 times. 10-8).  
 IT 138307-27-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep'n. of a nervous system agent)  
 RN 138307-27-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione,  
 8-(2-(4-[3-(trifluoromethyl)phenyl]-1-piperazinyl)ethyl)- (9CI) (CA INDEX NAME)

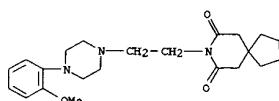


L14 ANSWER 175 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 .alpha.2B2 > .alpha.2B1 > .alpha.2A. All three .alpha.2-adrenoceptors showed the expected stereoselective binding for adrenaline enantiomers, the (+)-form being 7-10-fold less potent than the (-)-form. [3H]yohimbine was also used as radioligand. The data with this ligand were fully compatible with the [3H]II data. However, [3H]yohimbine appeared to label only .alpha.2B1- and .alpha.2B2-adrenoceptors presumably because it had too low an affinity for .alpha.2A-adrenoceptors. Apparently, 3 pharmacol. subtypes of .alpha.2-adrenoceptors are labeled by [3H]II in the rat kidney. Guanoxabenz and ARC 239 may be used in competition studies to delineate between these three .alpha.2-adrenoceptor subtypes.  
 IT 67339-62-2, ARC-239  
 RL: BIOL (Biological study)  
 (.alpha.2-adrenergic receptor classification with, in kidney)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isoquinolinodione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 176 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:598360 CAPLUS  
 DOCUMENT NUMBER: 115:198360  
 TITLE: Effects of serotonergic agents on  
 isolation-induced aggression  
 AUTHOR(S): White, Sheryl M.; Kucherik, Robert F.; Moyer,  
 John A.  
 CORPORATE SOURCE: CNS Div., Wyeth-Ayerst Res., Princeton, NJ,  
 08543-8000, USA  
 SOURCE: Pharmacol., Biochem. Behav. (1991), 39 (3), 729-36  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A series of serotonergic agents were assessed for their ability to antagonize isolation-induced aggression and disrupt performance in the rotarod motor coordination test. All compds. with 5-HT1A activity [buspirone, gepirone, ipsapirone, tandospirone (SM-3997), 8-OH-DPAT, Wy48,723, BMY7378, Wy47,846] reduced aggression at doses below those which produced debilitation in the rotarod motor coordination test. In addn., the 5-HT3 antagonist zacopride failed to attenuate aggression or produce debilitation at any of the doses tested; however, the 5-HT2 antagonist ritanserin inhibited aggressive behavior at a high dose which was not debilitating. Benzodiazepines (chlordiazepoxide, diazepam and lorazepam) and an antidepressant (desipramine) and an antipsychotic (haloperidol) reduced aggressive behavior only at debilitating doses. Activity at the 5-HT1A receptor, and possibly nonsedative anxiolytic activity, appears to be related to antagonism of isolation-induced aggression.  
 IT 21102-95-4, BMY-7378  
 RL: BIOL (Biological study)  
 (isolation-induced aggression response to, serotoninergic mechanisms)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspireo[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

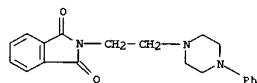
L14 ANSWER 176 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



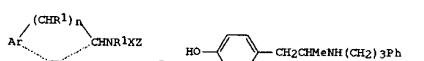
●2 HCl

L14 ANSWER 177 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:592801 CAPLUS  
 DOCUMENT NUMBER: 115:192801  
 TITLE: Preparation of substituted phenylisopropylamines and analogs as sigma receptor ligands for treatment of schizophrenia and psychoses  
 INVENTOR(S): Glennon, Richard A.  
 PATENT ASSIGNEE(S): Virginia Commonwealth University, USA  
 SOURCE: PCT Int. Appl., 101 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  
 -----  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 WO 9109594 A1 19910711 WO 1990-U57653 19901228  
 W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LX, MC, MG, MW, NO,  
 PL, RO, SD, SU, US  
 RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR,  
 IT, LU, ML, MR, NL, SE, SN, TD, TG  
 CA 2071897 A1 19910623 CA 1990-2071897 19901228  
 AU 9171684 A1 19910724 AU 1991-71684 19901228  
 AU 658134 B2 19950406  
 EP 507863 A1 19921014 EP 1991-902640 19901228  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE  
 JP 05503517 T2 19930610 JP 1991-502935 19901228  
 PRIORITY APPLN. INFO.: US 1989-459061 19891228  
 WO 1990-U57653 19901228  
 OTHER SOURCE(S): MARPAT 115:182001  
 G1

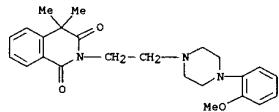
L14 ANSWER 177 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 phenyl-2-aminopropane. Also prep'd was the (+)-amine II.HBr (III). In sigma receptor binding assays the IC50 of III was 1.03 times. 10-8 M. I were subjected to sigma, PCP and dopamine receptor binding assays and the results showed very high binding to sigma receptor and very low binding to PCP and DA receptors, and thus I are useful for treatment of mental illness (no data) without the extrapyramidal side effects of traditional neuroleptic agents caused by binding to DA receptor.  
 IT 75000-24-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of a sigma receptor ligand)  
 RN 75000-24-7 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



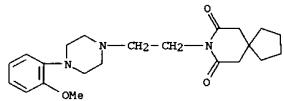
AB Title compds. I [Ar = (substituted) aryl or heteroaryl; R = H, C1-6 alkyl;  
 R1 = H, C1-6 alkyl, C1-6 alkoxy, Br, Cl, F, O or RR1 = morpholine,  
 piperazinyl, piperidinyl; n = 0-5; W = (CH2)p, 2H; p = 1-3; X =  
 (CH2)q; q = 1-6; (CH2)rC(=O)bond.C(CH2)r, (CH2)rCH:CH(CH2)r, (CH2)rCO(CH2)r,  
 (CH2)rY(CH2)r; r = 0-3; Y = O, S, C1-6 alkyl; Z = H, (substituted)  
 aryl or heteroaryl], are prep'd. PhCH2CH2CHO and (R)-(-)-PhCH2CH(NH2)Me in  
 MeOH were hydrogenated over Pt/C at room temp. to give  
 (R)-N-(3-phenylpropyl)-1-



L14 ANSWER 178 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:551496 CAPLUS  
 DOCUMENT NUMBER: 115:151496  
 TITLE: Identification and characterization of  
 .alpha.2D-adrenergic receptors in bovine pineal  
 gland  
 AUTHOR(S): Simonneaux, V.; Ebadi, M.; Bylund, D. B.  
 CORPORATE SOURCE: Med. Cent., Univ. Nebraska, Omaha, NE,  
 68198-6260, USA  
 SOURCE: Mol. Pharmacol. (1991), 40(2), 235-41  
 CODEN: MOPMA3; ISSN: 0026-895X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB By using [<sup>3</sup>H]rauwolscine, a selective .alpha.2-adrenergic receptor antagonist, .alpha.2-adrenergic receptor sites were identified in a mammalian pineal gland. [<sup>3</sup>H]Rauwolscine bound in a saturable manner to a single class of receptors, with an equil. dissoch. const. of 1.4 nM and a d. of 71 fmol/mg of protein, in crude synaptic membrane preps. from bovine pineal gland. Competition studies carried out with various adrenergic antagonists supported the conclusion that [<sup>3</sup>H]rauwolscine-binding sites were .alpha.2-adrenergic receptors. The bovine pineal .alpha.2-adrenergic receptor appears to represent a pharmacol. subtype distinct from the 3 currently proposed subtypes, i.e., .alpha.2B found in a human colonic adenocarcinoma cell line (HT29 cell), .alpha.2B found in rat lung, and .alpha.2C found in an opossum kidney cell line. However, the pharmacol. profile of the pineal .alpha.2 receptor resembles that found in the rat submaxillary gland. The bovine pineal receptor may represent a 4th pharmacol. subtype, which would be designated as .alpha.2D.  
 IT 67339-62-2, ARC-239  
 RL: BIOL (Biological study)  
 (.alpha.2D-adrenergic receptor binding by, in pineal gland)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolininedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

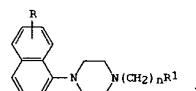
L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:528127 CAPLUS  
 DOCUMENT NUMBER: 115:128127  
 TITLE: Single-dose 8-OH-DPAT pretreatment does not induce tachyphylaxis to the 5-HT release-reducing effect  
 of 5-HT<sub>1A</sub> autoreceptor agonists  
 AUTHOR(S): Hjorth, Stephan  
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Goteborg, Goteborg, S-400 33, Swed.  
 SOURCE: Eur. J. Pharmacol. (1991), 199(2), 237-42  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB It has recently been suggested that central 5-HT<sub>1A</sub> autoreceptors are already desensitized after single-dose 5-HT<sub>1A</sub> agonist treatment. In turn, this would lead to an attenuated feedback suppression of transmitter release from 5-HT neurons, and thus to enhanced 5-HT synaptic transmission. In vivo brain microdialysis techniques were used in an attempt to test this hypothesis. Single-dose pretreatment with the ref. 5-HT<sub>1A</sub> receptor agonist 8-hydroxy-2-(di-n-propylamino)tetralin, 8-OH-DPAT, did not alter the baseline output of 5-HT in the rat ventral hippocampus 24 h later, and did not alter the release-reducing response to 5-HT<sub>1A</sub> agonist (8-OH-DPAT, ipsapirone or RMY 7378) challenge under the same conditions. Thus, the functional responsiveness of the 5-HT release-controlling 5-HT<sub>1A</sub> autoreceptors is maintained after bolus 8-OH-DPAT pretreatment. When related to the acute 8-OH-DPAT-induced redn. in raphe 5-HT<sub>1A</sub> radioligand binding d. recently reported by others, the present results are consistent with a large functional overcapacity of this 5-HT<sub>1A</sub> receptor population. The mechanism by which 5-HT<sub>1A</sub> receptor-mediated hypothermia and hyperphagia are rapidly attenuated by a previous large single dose of a 5-HT<sub>1A</sub> receptor agonist remains to be explained.  
 IT 21102-95-4, EMY 7378  
 RL: BIOL (Biological study)  
 (serotonin release by hippocampus response to, receptor desensitization in relation to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiron[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:514553 CAPLUS  
 DOCUMENT NUMBER: 115:114553  
 TITLE: 1-naphthylpiperazine derivatives, process for their preparation and pharmaceutical compositions containing them  
 INVENTOR(S): Lavieille, Gilbert; Laubie, Michel; Colpaert, Francis  
 PATENT ASSIGNEE(S): ADIR et Cie., Fr.  
 SOURCE: Eur. Pat. Appl., 58 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

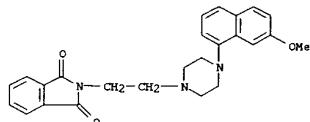
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 434561	A2	19910626	EP 1990-403688	19901220
EP 434561	A3	19910918		
EP 434561	B1	19951018		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2655988	A1	19910621	FR 1989-16882	19891220
FR 2655988	B1	19940522		
ZA 9009767	A	19911127	ZA 1990-9767	19901205
CA 2032713	AA	19910621	CA 1990-2032713	19901219
AU 9068235	A1	19910621	AU 1990-68235	19901219
AU 635369	B2	19900118		
JP 5324175	A2	19911220	JP 1990-403922	19901219
JP 00765395	B4	19940522		
US 5143916	A	19920901	US 1990-629824	19901219
AT 123241	E	19951115	AT 1990-403688	19901220
ES 2080815	T3	19960216	ES 1990-403688	19901220
US 5166157	A	19921124	US 1991-750821	19910827
US 5162324	A	19921110	US 1991-752060	19910829
US 5162321	A	19921110	US 1991-752063	19910829
US 5166156	A	19921124	US 1991-752065	19910829
PRIORITY APPLN. INFO.:			FR 1989-16882	19891220
			US 1990-629824	19901219

OTHER SOURCE(S): MARPAT 115:114553

GI



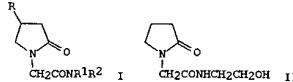
L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 AB Naphthylpiperazines I [n = 1-4; R = H, halogen, OH, alkyl, alkoxy;  
 R1 = NHCOR2, NHSO2R3, NHCONHR4, (un)substituted phthalimido,  
 benzisothiazole  
 dioxide, NBz2, imidazopyrimidinyl, azaspirodecyl; R2 = alkyl,  
 cycloalkyl, Ph,  
 Ph, substituted Ph, heteroaryl; R3 = alkyl, cycloalkyl, Ph,  
 substituted  
 Ph; R4 = alkyl, Ph, substituted Ph] were prepd. by various methods.  
 Thus 7-methoxy-1-naphthylpiperazine was treated with BrCH2CN, followed by  
 redn.  
 to the 2-aminoethyl deriv. and acylation to give I (n = 2, R =  
 7-OMe, R1 =  
 4-FC6H4CONH) which had better antihypertensive and neg. chronotropic  
 activity than flesinokan.  
 IT 135722-16-6P 135722-24-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 135722-16-6 CAPLUS  
 CN 1H-Indole-1,3(2H)-dione, 2-[2-[4-(7-methoxy-1-naphthalenyl)-1-  
 piperazinyl]ethyl], hydrochloride (9CI) (CA INDEX NAME)



●x HCl

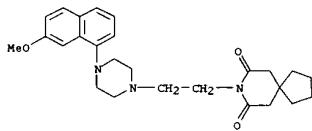
RN 135722-24-6 CAPLUS  
 CN 8-Azaspiro[4.5]decano-7,9-dione,  
 8-[2-[4-(7-methoxy-1-naphthalenyl)-1-  
 piperazinyl]ethyl], hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 181 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:492061 CAPLUS  
 DOCUMENT NUMBER: 115:92061  
 TITLE: Preparation of 2-pyrrolidone derivatives as  
 enhancers  
 for learning and memory  
 INVENTOR(S): Giannessi, Fabio; Ghirardi, Orlando; Misiti,  
 Domenico;  
 PATENT ASSIGNEE(S): Tinti, Maria Ornella; Scolastico, Carlo  
 Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.,  
 Italy  
 SOURCE: Eur. Pat. Appl., 20 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:  
 PATENT NO. KIND DATE APPLICATION NO. DATE  
 EP 408524 A1 19910116 EP 1990-830317 19900710  
 EP 408524 B1 19951108  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, LI, LU, NL, SE  
 AT 129996 E 19951115 AT 1990-830317 19900710  
 ES 2079469 T3 19960116 ES 1990-830317 19900710  
 JP 03048657 A2 19910301 JP 1990-185173 19900711  
 US 5061725 A 1991029 US 1990-551951 19900712  
 PRIORITY APPLN. INFO.: IT 1989-48180 19890712  
 OTHER SOURCE(S): MARPAT 115:92061  
 GI



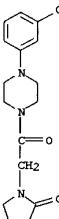
AB The title compds. I [R = H, OH; R1 = H; R2 = 2-aminoethyl,  
 2-(diisopropylamino)ethyl, 2-hydroxyethyl, etc.] were prepd. A  
 mixt. of  
 Me (2-oxopyrrolidin-1-yl)acetate and ethanamine was stirred at room  
 temp. for 20 h to give pyrrolidone deriv. II. I (R = R1 = H; R2 =  
 CH2CH2NH2) had memory-enhancing activity equal to that of piracetam.  
 IT 131028-02-9P 135459-98-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as memory enhancer)  
 RN 131028-02-9 CAPLUS  
 CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-  
 (9CI) (CA INDEX NAME)

L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

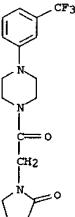


●x HCl

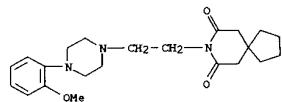
L14 ANSWER 181 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 135459-98-2 CAPLUS  
 CN Piperazine,  
 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[(3-(trifluoromethyl)phenyl)-  
 (9CI) (CA INDEX NAME)

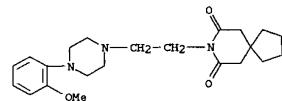


L14 ANSWER 182 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:485329 CAPLUS  
 DOCUMENT NUMBER: 115:85329  
 TITLE: BMY 7378 is an agonist at 5-HT1A receptors mediating hypotension and renal sympatho-inhibition in anesthetized cats  
 AUTHOR(S): Stubbs, Carole M.; Connor, Helen E.; Feniuk, Wasyl  
 CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Hertfordshire, SG12 0BJ, UK  
 SOURCE: Br. J. Pharmacol. (1991), 107(1), 113-16  
 CODEN: EJPBAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The putative 5-HT1A receptor antagonist BMY 7378 (3-100 .mu.g.cntdot.kg-1 i.v.) caused redns. in blood pressure, heart rate and efferent renal nerve activity in anesthetized cats. Similar effects were produced by the selective 5-HT1A receptor agonist, 8-hydroxy-2(di-n-propylamino)tetralin (8-OH-DPAT 1-10 .mu.g.cntdot.kg-1 i.v.). The sympatho-inhibitory effects of BMY 7378 and 8-OH-DPAT, but not those of clonidine were reversed by the non-selective 5-HT1A receptor antagonist, spiperone (1 mg.cntdot.kg-1 i.v.). It is concluded that BMY 7378 is an agonist at 5-HT1A receptors mediating hypotension and renal sympatho-inhibition in anesthetized cats.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (as serotonergic S1A receptor agonist, cardiovascular and renal sympathetic nerve response to)  
 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 183 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 heterobicyclic arylpiperazine selective 5-HT1A ligand, (-+)-flesinoxan, also failed to evoke STFs and attenuated the action of 8-OH-DPAT. The novel, putative 5-HT1A antagonists, BMY 7378 and NAN 190, abolished the action of 8-OH-DPAT and p-chloramphetamine. Thus, a high efficacy agonist action at 5-HT1A receptors is sufficient for the induction of STFs in the rat. This response offers a novel, robust, and quant. test for the in vivo characterization of drugs acting at 5-HT1A receptors.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (serotonergic S1A agonist-induced tail flick behavior antagonism by)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

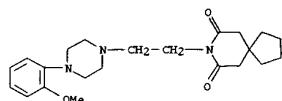


●2 HCl

L14 ANSWER 183 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:221898 CAPLUS  
 DOCUMENT NUMBER: 114:221898  
 TITLE: 5-Hydroxytryptamine (5-HT) 1A receptors and the tail-flick response. I. 8-Hydroxy-2-(di-n-propylamino)tetralin hydrobromide-induced spontaneous tail-flicks in the rat as an in vivo model of receptor-mediated activity  
 AUTHOR(S): Millan, Mark J.; Bervoets, Karin; Colpaert, Francis C.  
 CORPORATE SOURCE: Neurobiol. Div., Fondax, Puteaux, 92800, Fr.  
 SOURCE: J. Pharmacol. Exp. Ther. (1991), 256(3), 973-82  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB This study characterizes a novel behavioral response as a potential in vivo model of 5-HT1A receptor-mediated activity. In rats restrained in horizontal cylinders, the selective 5-HT1A agonist 8-hydroxy-2-(di-n-propylamino)tetralin-HBr (8-OH-DPAT) dose-dependently (0.04-10.0 mg/kg, s.c.) elicited spontaneous tail-flicks (STFs). This action was mimicked by other ligands possessing high affinity and high efficacy at 5-HT1A sites: RU 24969, lisuride, (+)-LSD, and 5-methoxy-N,N-dimethyltryptamine hydrogen oxalate. The response could not be elicited by CGS 12066B, mCPP [1-(3-chlorophenyl)-piperazine-2-HCl], TFMPP, MK 212, quipazine, and (-+)-2,5-dimethoxy-4-iodophenyl-2-aminopropane-HCl, which act in vivo as agonists at 5-HT1B, 5-HT1C and/or 5-HT2 receptors, or by the 5-HT3 agonist, 2-methyl-5-HT. p-Chloroamphetamine, which releases endogenous 5-HT, also evoked STFs; in contrast, d-amphetamine, a preferential releaser of catecholamines, was inactive as were agonists and antagonists at .alpha.1-, .alpha.2-, .beta.1-, .beta.2-, and dopamine D1 and D2 sites. 8-OH-DPAT-elicited STFs were blocked by the 5-HT1/2 antagonist, methiothepin, but not by the 5-HT1C/5-HT2 antagonists, mianserin, ritanserin, and ICI 169,369 nor by the 5-HT3 antagonists, GR 38032F, ICS 205,930, and MDL 72222. .beta.-Blockers with high 5-HT1A affinity i.e., (-)-alprenolol, (-+)-isomethane and, stereoselectively, (-) but not (+)-pinadol, blocked the action of 8-OH-DPAT. Spiperone and spiroxatrine, D2 antagonists with high 5-HT1A affinity, also inhibited 8-OH-DPAT-induced STFs. Selective .beta.-blockers and D2 antagonists with low 5-HT1A affinity were inactive. 5-HT1A partial agonists, the pyrimidinylpiperazines buspirone, gepirone, and ipsapirone, the halogenated phenylpiperazine LY 165,163, and the benzodiazoxine MDL 72832 did not elicit STFs and antagonized the effect of 8-OH-DPAT. The

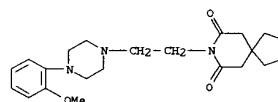
L14 ANSWER 184 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:178855 CAPLUS  
 DOCUMENT NUMBER: 114:178855  
 TITLE: 5-Hydroxytryptamine (HT)1A receptors and the tail-flick response. II. High efficacy 5-HT1A agonists attenuate morphine-induced antinociception in mice in a competitive-like manner  
 AUTHOR(S): Millan, M. J.; Colpaert, F. C.  
 CORPORATE SOURCE: Neurobiol. Div., Fondax, Puteaux, 92800, Fr.  
 SOURCE: J. Pharmacol. Exp. Ther. (1991), 256(3), 983-92  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB This study examined the influence of s.c. administration of HT1A agonists upon the antinociceptive action of s.c. injected morphine in tail-flick tests to noxious heat and pressure. The selective 5-HT1A agonist, (-+)-8-hydroxy-dipropylaminotetralin-Br (8-OH-DPAT), dose-dependently antagonized morphine-induced antinociception (MIA) without affecting the latency to respond when applied alone. In the presence of increasing doses of 8-OH-DPAT (0.16-0.63 mg/kg), the morphine dose-response curve was shifted progressively to the right and the maximal effect of morphine was not altered; Schild anal. yielded a slope of close to -1.0. 8-OH-DPAT both prevented and reversed the action of morphine. The action of 8-OH-DPAT was reversible (at 24 h). In contrast, 8-OH-DPAT neither blocked morphine-induced Straub tail nor pptd. withdrawal in morphine-dependent animals; thus, it lacked opioid-antagonist properties. The antagonism of MIA by 8-OH-DPAT was mimicked by addnl. drugs acting as high efficacy 5-HT1A agonists: lisuride, 5-methoxy-N,N-dimethyltryptamine hydrogen oxalate, RU 24969 and d-LSD. In contrast, the 5-HT1B/1C agonist TFMPP and the 5-HT1C/2 agonist (-+)-2,5-dimethoxy-4-iodophenyl-2-aminopropane-HCl were ineffective. The putative selective 5-HT1A antagonists BMY 7378 and spiperone did not reduce MIA. Indeed, BMY 7378 blocked the ability of 8-OH-DPAT to antagonize MIA. Under the present conditions, agonists and antagonists at adrenergic and dopaminergic receptors did not attenuate MIA. These data show that, over a certain range of doses, the systemic administration of 8-OH-DPAT and other high efficacy 5-HT1A agonists functionally antagonizes the antinociceptive action of systemically applied morphine in a competitive-like manner. It is suggested that 5-HT1A receptors play an important role in the modulation of opioidergic antinociceptive mechanisms.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)

L14 ANSWER 184 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (serotoninergics 5<sub>1</sub>A agonist antagonism of morphine analgesia blockade by)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 185 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 1991:178780 CAPLUS  
 DOCUMENT NUMBER: 114:178780  
 TITLE: intra-raphe  
 Differential behavior activation following infusion of 5-HT1A receptor agonists  
 AUTHOR(S): Higgins, Guy A.; Elliott, Peter J.  
 CORPORATE SOURCE: Glaxo Neuropharmacol., Glaxo Group Res. Ltd., Ware/Hertfordshire SG12 0DP, UK  
 SOURCE: Eur. J. Pharmacol. (1991), 193(3), 351-6  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Microinfusion of the selective 5-HT1A receptor agonist, 8-hydroxy-(di-N-propylamino)tetralin (8-OHDPAT), into the dorsal raphe nucleus (DRN) produced a marked behavioral hypoactivity and flat body posture. Injections of similar doses into the median raphe nucleus (MRN) elicited hyperactivity but no postural change. Redns. in rearing and grooming were also obsd. after DRN and MRN infusions of 8-OHDPAT. The behavioral profiles of other 5-HT1A selective compds., gepirone and BMY 7378 were found to be similar to 8-OHDPAT. The contrasting behavioral profiles of the 5-HT1A agents obsd. after DRN or MRN microinfusion are probably related to the differential innervation of forebrain structures by each raphe nucleus. Thus, the present data confirms and extends previous results illustrating the influence of 5-HT systems on motor behavior in the rat and identifies unique behavioral profiles following activation of the DRN and MRN.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (behavioral response to intra-raphe administration of serotoninergic agonists for)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

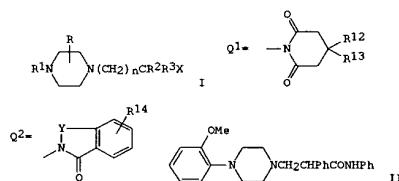
L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:143444 CAPLUS  
 DOCUMENT NUMBER: 114:143444  
 TITLE: Preparation of 1-aryl-4-carboxyalkylpiperazines and related compounds as serotoninergic antagonists  
 INVENTOR(S): Cliffe, Ian Anthony  
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., UK  
 SOURCE: Eur. Pat. Appl., 33 pp.  
 CODEN: EPXXDW

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 395312	A2	19901031	EP 1990-304250	19900420
EP 395312	A3	19910508		
EP 395312	B1	19920512		
R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE CA 2015034	AA	19901022	CA 1990-2015034	19900420
AU 9053779	AU	19901025	AU 1990-53779	19900420
AU 619678	B2	19920130		
GB 2230781	A1	19901031	GB 1990-8925	19900420
GB 2230781	B2	19930428		
HU 54666	A2	19910328	HU 1990-2504	19900420
DD 296921	A2	19911219	DD 1990-339954	19900420
ZA 9003019	A	19911224	ZA 1990-3019	19900420
ZA 9003020	A	19911224	ZA 1990-3020	19900420
DD 979768	A5	19920103	DD 1990-332055	19900420
IL 94151	A1	19950831	IL 1990-94151	19900420
AT 179973	E	19990515	AT 1990-304250	19900420
ES 2130116	T3	19990701	ES 1990-304250	19900420
JP 03011059	A2	19910118	JP 1990-106299	19900421
JP 3036786	B2	20000424		
US 5364849	A	19941115	US 1992-911996	19920710
GB 2255976	A1	19921125	GB 1992-15425	19920720
GB 2255976	B2	19921125		
US 5382583	A	19950117	US 1992-998887	19921229
US 5420812	A	19940823	US 1993-1428	19930107
US 5420778	A	19950530	US 1994-248124	19940524
US 5541326	A	19960730	US 1995-159000	19951114
PRIORITY AFFLN. INFO.:				
GB 1989-9209	A	19890422		
GB 1989-24323	A	19891028		
US 1990-511150	B2	19900419		
GB 1990-8925	A3	19900420		
US 1991-748496	B1	19910822		
US 1991-748497	B1	19910822		
US 1991-756932	B1	19910909		
US 1992-911996	A3	19920710		
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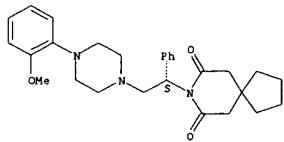
OTHER SOURCE(S): MARPAT 114:143444  
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L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

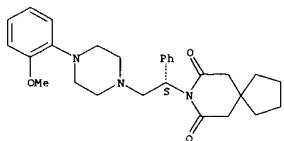


AB The title compds. [I; R = H, alkyl; R1 = aryl, N-contg. heteroaryl; R2 = H, alkyl; R3 = aryl, alkyl, arylalkyl; X = O2CR10, CO2R6, CONR5R9, OCO2R6, NR4COR6, Q1, Q2, etc.; R4 = H, alkyl; R6 = alkyl, cycloalkyl, arylalkyl; R9 = H, alkyl, cycloalkyl, aryl, arylalkyl, 8-azaspiro[4.5]deca-7,9-dione-8-yl-alkyl, etc.; R12, R13 = alkyl; R12R13C = cycloalkyl; R14 = H, halo, alkyloxy; Y = CO, SO2; n = 1, 2] were prep'd. Thus, 1-(2-methoxyphenyl)piperazine was refluxed 18 h with atropic acid in EtOH to give alpha-[1-(4-(2-methoxyphenyl)piperazinyl)methyl]benzeneacetic acid. The latter in CH2Cl2 was treated with carbonyldiimidazole and then aniline to give title compd. II. I. bound to rat hippocampal 5-HT1A receptors with IC50's of 8-127 nm.  
 IT 132708-63-5P 132709-11-6P  
 RL SPP (Synthetic preparation); PREP (Preparation)  
 (prep. of, as serotoninergic antagonist)  
 RN 132708-63-5 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione,  
 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-phenylethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

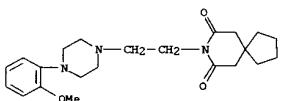


RN 132709-11-6 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione,  
 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-  
 1-phenylethyl]-, dihydrochloride, (S)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry.



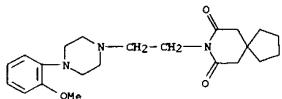
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L14 ANSWER 187 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:136585 CAPLUS  
 DOCUMENT NUMBER: 114:136585  
 TITLE: The effect of putative 5-HT1A receptor antagonists on 8-OH-DPAT-induced hypothermia in rats and mice  
 AUTHOR(S): Moser, Paul C.  
 CORPORATE SOURCE: Merrell Dow Res. Inst., Strasbourg, F-67009, Fr.  
 SOURCE: Eur. J. Pharmacol. (1991), 193(2), 165-72  
 CODEN: EUPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of 3 putative 5-HT1A receptor antagonists (NAN-190, BMY 7378, and WB 4101) were studied on the hypothermia induced by 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT). In order to control for the  $\alpha$ . $\alpha$ .1-adrenoceptor antagonist activity of NAN-190 and WB 4101, the effects of prazosin were also examined. Both NAN-190 and WB 4101 lowered body temp. in the mouse. This effect appeared to be due to their  $\alpha$ . $\alpha$ .1-adrenoceptor antagonist effects, as prazosin had a similar profile. Neither NAN-190, WB 4101 nor prazosin antagonized the hypothermic effects of 8-OH-DPAT. BMY 7378 slightly lowered body temp. but to a lesser extent than 8-OH-DPAT and, in contrast to the other comds. studied, also prevented a fall in body temp. on injection of 8-OH-DPAT. In the rat there was much less interference from  $\alpha$ . $\alpha$ .1-adrenoceptor antagonist activity as both NAN-190 and prazosin only slightly reduced body temp. In this species, however, NAN-190 showed marked antagonist activity against 8-OH-DPAT hypothermia. This was not due to  $\alpha$ . $\alpha$ .1-adrenoceptor antagonist activity as prazosin had no effect. In the rat, as in the mouse, BMY 7378 had a partial agonist profile, whereas WB 4101 behaved essentially as an agonist. These results suggest that NAN-190 is a pure antagonist of 8-OH-DPAT-induced hypothermia and that BMY 7378 and WB 4101 are, resp., a partial agonist and an antagonist in this test. The rat seems to be the better species for the study of 5-HT1A receptors using 8-OH-DPAT-induced hypothermia as it is less affected by  $\alpha$ . $\alpha$ .1-adrenoceptor antagonist activity and because the mouse model fails to demonstrate an interaction of NAN-190 with 5-HT1A receptors.  
 IT 21102-95-4, BMY7378  
 RL: BIOL (Biological study)  
 (hydroxymethylamino)tetralin rcdn. in body temp. response to, serotonin receptor subtype and species in relation to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

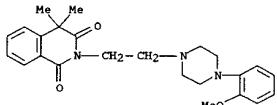
L14 ANSWER 188 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:136473 CAPLUS  
 DOCUMENT NUMBER: 114:136473  
 TITLE: Agonist action at 5-HT1C receptors facilitates 5-HT1A receptor-mediated spontaneous tail-flicks in the rat  
 AUTHOR(S): Bervoets, Karin; Millan, Mark J.; Colpaert, Francis C.  
 CORPORATE SOURCE: Neurobiol. Div., FONDAX, Putaux, 92800, Fr.  
 SOURCE: Eur. J. Pharmacol. (1990), 191(2), 185-95  
 CODEN: EUPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In rats lightly restrained in plastic cylinders, s.c. administration of the selective, high-efficacy 5-HT1A receptor agonist 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT) induced spontaneous tail flicks. The putative 5-HT1B receptor agonist CGS 12066B, the mixed 5-HT1B/1C receptor agonists 1-(3-(trifluoromethyl)phenyl)piperazine (TMPPF) and 1-(3-chlorophenyl)piperazine (mCPP), the 5-HT1C/2 receptor agonist ((+,-)-1-(2,5-dimethoxy-4-iodophenyl)-2-amino propane (DOI), and the 5-HT1B/1C/2 receptor agonist quipazine did not elicit tail flicks when applied alone. However, TMPPF, mCPP, DOI, and quipazine, but not CGS 12066B, each potentiated the action of 8-OH-DPAT. Further, in the presence of TMPPF, mCPP, and DOI, the dose-receptor curve for the induction of tail flicks by 8-OH-DPAT was both steeper and shifted to the left. Tail flicks induced by another high-efficacy 5-HT1A receptor agonist, lisuride, were also enhanced by TMPPF, mCPP, and DOI. The 5-HT1B receptor partial agonists buspirone and (+,-)-flesinoxan evoked tail-flicks only in the presence of TMPPF, mCPP, or DOI. The mixed 5-HT1C/2 receptor antagonists ritanserin and ICI 169,369 did not modify the action of 8-OH-DPAT alone but abolished the potentiation of 8-OH-DPAT-induced tail flicks by DOI and TMPPF. Further, the selective 5-HT1A receptor antagonist BMY 7378 blocked tail flicks induced by both 8-OH-DPAT alone and 8-OH-DPAT plus DOI or TMPPF. A common property of those drugs potentiating 8-OH-DPAT-induced tail flicks is an agonist action at 5-HT1C receptors and the data indicate that it is this mechanism which underlies the facilitation of tail flicks.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (behavior induced by 5-HT1A and 5-HT1C receptor agonist inhibition by)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

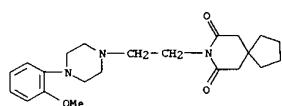
L14 ANSWER 189 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:36477 CAPLUS  
 DOCUMENT NUMBER: 114:36477  
 TITLE: Functional characterization of neuronal pre- and postsynaptic alpha.2-adrenoceptor subtypes in guinea pig submucosal plexus  
 AUTHOR(S): Shen, X. Z.; Barajas-Lopez, C.; Surprenant, A.  
 CORPORATE SOURCE: Vollum Inst., Oregon Health Sci. Univ., Portland, OR,  
 97201, USA  
 SOURCE: Br. J. Pharmacol. (1990), 101(4), 925-31  
 CODEN: BJPCBM; ISSN: 0007-1188  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The .alpha.2-adrenoceptors on cell bodies of submucosal neurons, on presynaptic cholinergic nerve terminals innervating submucosal neurons, and on presynaptic sympathetic fibers innervating submucosal arterioles were characterized in functional studies by use of subtype selective ligands. Both membrane hyperpolarization and presynaptic inhibition of nicotinic excitatory synaptic potentials (e.p.s.ps) produced by UK 14304 were similarly antagonized by idazoxan, yohimbine, SKF 104078, WB 4101, and ARC 239. Antagonism was competitive and dissoon. consts. were the same for both effects. Vasoconstriction of submucosal arterioles in response to stimulation of the sympathetic nerves (20 Hz for 2 s) was inhibited by UK 14304 and clonidine; concns. producing half-max. responses were 6 and 10 nM, resp. Idazoxan, yohimbine, WB 4101, and SKF 104078 antagonized this action, with dissoon. consts. similar to those for antagonism of the postsynaptic membrane hyperpolarization and presynaptic inhibition of nicotinic e.p.s.ps. Oxymetazoline was a partial agonist when membrane hyperpolarization or presynaptic inhibition of nicotinic e.p.s.ps were measured but a full agonist when presynaptic inhibition of sympathetically-mediated arteriolar vasoconstriction was measured. As an agonist, oxymetazoline produced half-max. responses at 80-120 nM; the dissoon. const. for oxymetazoline as an antagonist was 130 nM. Neither reserpine nor chlorpromazine (up to 30 .mu.M) altered any of the 3 responses to .alpha.2-adrenoceptor agonists. Thus, .alpha.2-adrenoceptors present on submucosal neuronal cell bodies, on presynaptic cholinergic nerve terminals, and on presynaptic sympathetic nerve terminals are the .alpha.2A subtype. However, functional characterization of this subtype differs from that provided by ligand binding studies.  
 IT 67339-62-2, ARC 239

L14 ANSWER 189 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RL: BIOL (Biological study)  
 .alpha.2-adrenoceptor mediated submucosal plexus activity stimulation  
 by UK 14304 inhibition by)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isoquinolininedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 190 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:35858 CAPLUS  
 DOCUMENT NUMBER: 114:35858  
 TITLE: Behavioral effects of serotonin agonists and antagonists in the rat and marmoset  
 AUTHOR(S): Higgins, G. A.; Hayes, A. G.  
 CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Herts., SG12 0DP, UK  
 SOURCE: Neuropharmacology (1990), 29(10), 949-56  
 CODEN: NEPHBW; ISSN: 0028-3908  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The present study was conducted to investigate the effects of various 5-HT agonists and antagonists on motor behavior in rats and marmosets. Various motor-based responses were assessed after central or peripheral administration of 5-HT agents to rats and marmosets. Drugs acting as agonists at the 5-HT1A receptor (8-OHDPAT, gepirone, BMY-7378, NAN-190, PAPP (LY165163) and flesinoxan) and 5-HT2/1C receptors (DOI) were found to reverse neuroleptic-induced catalepsy in the rat, whereas 5-HT2/1C antagonists (mianserin, ritanserin and ICI-70,809) and the 5-HT1 antagonist ((+-)pindolol) increased catalepsy. Agonists acting at 5-HT3 receptors (phenylbiguanide and 2-methyl-5-HT) had no effect on catalepsy. The putative 5-HT1A antagonist, ((+-)pindolol, attenuated the reversal of catalepsy by 8-OHDPAT. Although both 8-OHDPAT and BMY-7378 were tested, only the latter was found to reduce apomorphine-induced stereotypy. Bilateral or unilateral infusions of 8-OHDPAT, BMY-7378 or pindolol into the substantia nigra of non-lesioned rats had no effect on spontaneous locomotor or rotational activity, resp. However, 8-OHDPAT and BMY-7378 were found to increase or decrease motor activity, after injection into the median or dorsal raphe nuclei, resp. Finally, 8-OHDPAT and BMY-7378 were found to be inactive against MPTP-induced bradykinesia in the marmoset. It is concluded that both 5-HT1A and 5-HT2/1C receptors are involved in the anti-cataleptic effects of 5-HT agents. The 5-HT1A receptors are probably situated within the raphe, whereas the location of the 5-HT2/1C receptors remains undetd.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (behavior response to, brain serotonergic receptors in)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azapiro[4.5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

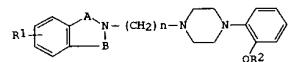
L14 ANSWER 190 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
piperazinyl)ethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

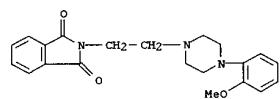
L14 ANSWER 191 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1991:12226 CAPLUS  
DOCUMENT NUMBER: 114:12226  
TITLE: Preparation of N,N'-disubstituted piperazines for treatment of dysuria  
INVENTOR(S): Hirokori, Isamu; Yoko, Tsuruoka, Takashi; Inoue, Shigeharu; Meiji Seika Kaisha, Ltd., Japan  
PATENT ASSIGNEE(S): Jpn. Kokai Tokkyo Koho, 7 pp.  
SOURCE: CODEN: JKOKAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02184667	A2	19900719	JP 1989-5482	19890111
OTHER SOURCE(S): MARPAT 114:12226 GI				

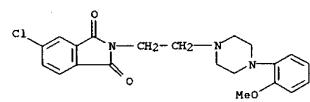


AB Pharmaceuticals for treatment of dysuria contain the title compds. I  
(A = CH<sub>2</sub> CO; B = CO, SO<sub>2</sub>; R1 = H, halo; R2 = C1-3 alkyl; n = 2-4) or their pharmaceutically acceptable salts as active ingredients. The treatment of 1-(2-methoxyphenyl)piperazine with 2-(2-bromoethyl)phthalimidine and Na<sub>2</sub>CO<sub>3</sub> in DMF at room temp. for 16 h gave 73% 2-[4-(2-methoxyphenyl)piperazinethyl]phthalimidine (II), which blocked alpha-1-adrenalin receptor in aorta and urethra with pA<sub>2</sub> of 8.1 and 8.2, resp., vs. 8.6 and 8.1, for the control contg. prazosin, resp. Tablets were formulated contg. II 10.0, lactose 86.8, corn starch 37.0, poly(vinylpyrrolidone) 5.0, and Mg stearate 1.2 mg. IT 99718-67-9P 130976-13-5P  
RL: PREP (Preparation)  
(prepn. of, for treatment of dysuria)  
RN 99718-67-9 CAPLUS  
CN 1H-Isocindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

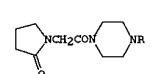
L14 ANSWER 191 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 130976-13-5 CAPLUS  
CN 1H-Isocindole-1,3(2H)-dione, 5-chloro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1991:6443 CAPLUS  
DOCUMENT NUMBER: 114:6443  
TITLE: Potential nootropic agents: synthesis of a series of (2-oxo-1-pyrrolidinyl)acetic acid piperazides  
AUTHOR(S): Valenta, Vladimír; Sindelář, Karel; Holubek, Jiří; Ryška, Miroslav; Krejčí, Ivan; Blábač, Antonín; Protiva, Miroslav  
CORPORATE SOURCE:  
SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 60, Czech. Collect. Czech. Chem. Commun. (1990), 55(6), 1613-29  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 114:6443  
GI

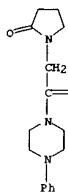


AB The title compds., e.g., I (R = Me, CH<sub>2</sub>CH<sub>2</sub>OMe, CH<sub>2</sub>Ph, CO<sub>2</sub>Et, Ph, substituted Ph) were prep'd. by heating Et (2-oxo-1-pyrrolidinyl)acetate with a series of N-monosubstituted piperazines. The propionamides' e.g., I (CH<sub>2</sub>CH<sub>2</sub>CONH<sub>2</sub>), were obtained by reactions of the acid chlorides with 3-(1-piperazinyl)propionamide. I (R = Me, CH<sub>2</sub>CH<sub>2</sub>OMe) proved more active than piracetam by their antimnesic effects in rats, by antagonizing the brain-damaging effects of cycloheximide in infantile rats, and by their potentiation of the effects of anticonvulsant agents.

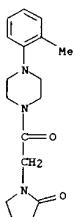
IT 131027-95-7P 131027-96-8P 131027-97-9P  
131027-98-0P 131028-00-7P  
131028-01-8P 131028-02-9P 131028-23-4P  
131028-24-5P 131028-25-6P 131028-26-7P  
131028-27-8P 131028-28-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

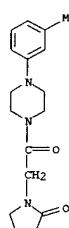
RN 131027-95-7 CAPLUS  
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



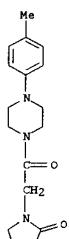
RN 131027-96-8 CAPLUS  
CN Piperazine, 1-(2-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-  
(9CI) (CA INDEX NAME)



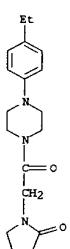
RN 131027-97-9 CAPLUS  
CN Piperazine, 1-(3-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-  
(9CI) (CA INDEX NAME)



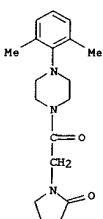
RN 131027-98-0 CAPLUS  
CN Piperazine, 1-(4-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)  
(CA INDEX NAME)



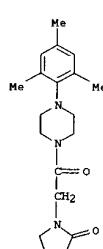
RN 131027-99-1 CAPLUS  
CN Piperazine, 1-(4-ethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)  
(CA INDEX NAME)



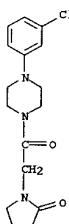
RN 131028-00-7 CAPLUS  
CN Piperazine, 1-(2,6-dimethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-  
(9CI) (CA INDEX NAME)



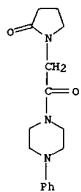
RN 131028-01-8 CAPLUS  
CN Piperazine,  
1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-(2,4,6-trimethylphenyl)-  
(9CI) (CA INDEX NAME)



RN 131028-02-9 CAPLUS  
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)  
(CA INDEX NAME)

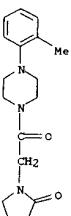


RN 131028-23-4 CAPLUS  
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl-,  
monohydrochloride  
(9CI) (CA INDEX NAME)



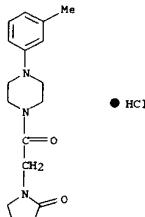
● HCl

RN 131028-24-5 CAPLUS  
 CN Piperazine, 1-(2-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

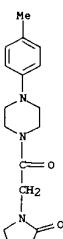


● HCl

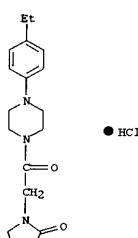
RN 131028-25-6 CAPLUS  
 CN Piperazine, 1-(3-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



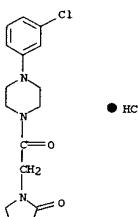
RN 131028-26-7 CAPLUS  
 CN Piperazine, 1-(4-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



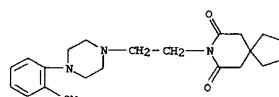
RN 131028-27-8 CAPLUS  
 CN Piperazine, 1-(4-ethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 131028-28-9 CAPLUS  
 CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



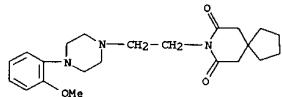
L14 ANSWER 193 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 131029-604753 CAPLUS  
 DOCUMENT NUMBER: 113:204753  
 TITLE: 5-HT1A agonist effects on punished responding of squirrel monkeys  
 AUTHOR(S): Gleeson, S.; Barrett, J. E.  
 CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20889-4799, USA  
 SOURCE: Pharmacol., Biochem. Behav. (1990), 37(2), 335-7  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Buspirone and other drugs that act as 5-HT1A agonists appear to be effective anxiolytics in humans, yet their anticonflict effects, though robust in pigeons, are equivocal in rodents. In the present study the effects of the benzodiazepine midazolam and a series of 5-HT1A agonists were examined on punished responding of squirrel monkeys. Lever presses were reinforced according to a fixed-interval 3-min schedule; in addition, each 30th lever press was punished. Midazolam produced large increases in response rates, whereas none of the 5-HT1A compounds produced any increases in responding. Most of these drugs decreased response rates at the higher doses examined. Although the reasons for the discrepancy between species in the anticonflict effects of serotonergic anxiolytics cannot be specified, the different anatomical distribution of 5-HT1A binding sites across species may suggest a different functional role for this receptor.  
 IT 21102-95-4, RMY 7378  
 RL: BIOL (Biological study)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

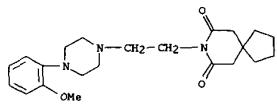
L14 ANSWER 194 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1990:471240 CAPLUS  
 DOCUMENT NUMBER: 113:71240  
 TITLE: BMY 7378: partial agonist at spinal cord 5-HT1A receptors  
 AUTHOR(S): Zemlan, Frank P.; Zieleniewski-Murphy, Anne; Murphy, R. Maureen; Behbehani, Michael M.  
 CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH, 45267-0559, USA  
 SOURCE: Neurochem. Int. (1990), 16(4), 515-22  
 DOCUMENT TYPE: CODEN: NEUDIS; ISSN: 0197-0186  
 LANGUAGE: Journal English  
 AB Recent data indicate that BMY 7378 demonstrates high affinity, selectivity and low intrinsic activity at hippocampal 5-HT1A receptors, suggesting that BMY 7378 may represent the first selective 5-HT1A functional antagonist. The present study examined the agonist and antagonist properties of BMY 7378 at spinal cord 5-HT1A receptors. In electrophysiologic studies, iontophoretic administration of either the 5-HT1A agonist 8-OH-DPAT (43.8 nA) or BMY 7378 (46.3 nA) significantly inhibited the firing rate of wide-dynamic-range dorsal horn units indicating that BMY 7378 demonstrates significant intrinsic activity at spinal cord 5-HT1A receptors. Concomitant BMY 7378 and 8-OH-DPAT administration identified no BMY 7378 ejection current (20-100 nA) which antagonized the 8-OH-DPAT-induced inhibition of dorsal horn unit activity. In behavioral studies in the spinal rat, 8-OH-DPAT increased the animals' sensitivity to noxious levels of mech. stimulation (ED50 = 269 nmol/kg) as did BMY 7378 (ED50 = 295 nmol/kg) with no statistically significant differences in the maximal response (Ymax) obesd. Concomitant BMY 7378 and 8-OH-DPAT administration identified no BMY 7378 dose (10-1100 nmol/kg) which blocked the hyperalgesic effect of 8-OH-DPAT; rather, each drug produced similar effects which were additive. Further, the 5-HT1A-agonist effects of BMY 7378 were blocked by the 5-HT1A antagonist spiperone. Therefore, both the electrophysiologic and reflex data indicate that BMY 7378 possesses intrinsic activity at spinal cord 5-HT1A receptors, and like 8-OH-DPAT is a partial agonist at these receptors. Differences in BMY 7378 intrinsic activity at spinal cord as opposed to hippocampal 5-HT1A receptors are discussed in terms of regional differences in G-proteins coupled to 5-HT1A receptors in

L14 ANSWER 194 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 these two CNS regions.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (as serotoninergic 5IA receptor partial antagonist, in spinal cord)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



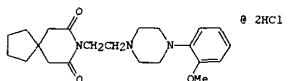
●2 HCl

L14 ANSWER 195 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1990:471154 CAPLUS  
 DOCUMENT NUMBER: 113:71154  
 TITLE: RU 24969-induced emesis in the cat: 5-HT1 sites other than 5-HT1A, 5-HT1B or 5-HT1C implicated  
 AUTHOR(S): Lucot, James B.  
 CORPORATE SOURCE: Dep. Pharmacol., Wright State Univ., Dayton, OH, 45435, USA  
 SOURCE: Eur. J. Pharmacol. (1990), 180(2-3), 193-9  
 DOCUMENT TYPE: CODEN: EUPHHAZ; ISSN: 0014-2999  
 LANGUAGE: Journal English  
 AB RU 24969 was administered s.c. to cats and found to elicit with a maximally ED of 1.0 mg/kg. 5-Methoxytryptamine was found to have lower efficacy and to produce a higher incidence of non-specific effects while trifluoromethylphenylpiperazine was devoid of emetic effects. The emesis elicited by 1.0 mg/kg of RU 24969 was not altered by pretreatment with phenothiazine, haloperidol, yohimbine or (-)-propranolol, indicating that catecholamines played no role in this response. The emesis was prevented by metergoline and methysergide but not by ketanserin, cyproheptadine, mesergoline, ICS 205,930, methiothepin, trimethobenzamide or BMY 7378. An indirect argument is presented that implicates a role for 5-HT1D sites. This conclusion must remain tentative until drugs selective for this site are synthesized and tested. The emesis was also prevented by 8-hydroxy-2-(di-n-propylamino)tetralin, confirming that this drug has a general antiemetic effect in cats.  
 IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (RU 24969-induced emesis response to, serotonin receptor sites in relation to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

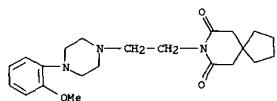
L14 ANSWER 196 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1990:191749 CAPLUS  
 DOCUMENT NUMBER: 112:191749  
 TITLE: Further investigation of the in vivo  
 pharmacological properties of the putative 5-HT1A antagonist, BMY  
 7378  
 AUTHOR(S): Sharp, Trevor; Backus, Lisa L.; Hjorth, Stephan;  
 Bramwell, Steven R.; Grahame-Smith, David G.  
 CORPORATE SOURCE: Dep. Clin. Pharmacol., Radcliffe Infirmary, Oxford,  
 OX2  
 SOURCE: GME, UK  
*Eur. J. Pharmacol.* (1990), 176(3), 331-40  
 DOCUMENT TYPE: CODEN: EJPRAZ; ISSN: 0014-2999  
 LANGUAGE: Journal  
 English  
 GI



I

AB The present study examined the action of the putative 5-HT1A antagonist, BMY 7378 (I) on central pre- and postsynaptic 5-HT1A function in the rat in vivo. Unlike the direct acting 5-HT1A agonist 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT), BMY 7378 (0.25-5 mg/kg s.c.) did not induce the full postsynaptically mediated 5-HT behavioral syndrome (forepaw treading, head weaving, flat body posture, hindlimb abduction). Indeed, the maximal 5-HT behavioral syndrome scores for BMY 7378 were about 10% of those for 8-OH-DPAT. Following pretreatment, however, BMY 7378 (0.5 mg/kg concn.-dependently (0.25-5 mg/kg s.c.) reduced to undetectable levels forepaw treading and head weaving induced by 8-OH-DPAT (0.75 mg/kg s.c.). BMY 7378 also inhibited stereotypy and locomotor activity induced by 0.5 mg/kg apomorphine at 5 mg/kg. In contrast to its apparent 5-HT1A antagonist properties in the behavioral expts., BMY 7378 caused a marked and concn.-dependent (0.01-1.0 mg/kg s.c.) decrease of 5-HT release in ventral hippocampus of the anesthetized rats as detected by brain microdialysis. This effect of BMY 7378 had a similar onset and duration of action but with slightly reduced efficacy compared to that previously described for 8-OH-DPAT. As with 8-OH-DPAT, the inhibitory effect of BMY

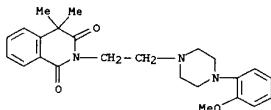
L14 ANSWER 196 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 not 7378 on 5-HT release was attenuated by pretreatment with the 5-HT1 receptor/.beta.-adrenoceptor antagonist pindolol (1 mg/kg s.c.) but  
 its counterpart propranolol (20 mg/kg s.c.). Pretreatment with a combination of the .beta.1- and .beta.2-adrenoceptor antagonists metoprolol (4 mg/kg s.c.) and ICI 118551 (4 mg/kg s.c.), resp., did  
 not alter the 5-HT response to BMY 7378. BMY 7378 is a mixed  
 agonist/antagonist at central 5-HT1A receptors.  
 IT 22102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (serotonergic SIA receptors of brain response to, mixed  
 agonist-antagonist activity in relation to)  
 PN 22102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]deca-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-, dihydrochloride (SC1) (CA INDEX NAME)



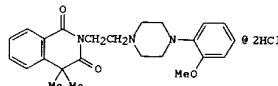
●2 HCl

L14 ANSWER 197 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1990:152352 CAPLUS  
 DOCUMENT NUMBER: 112:152352  
 TITLE: Subtypes of .alpha.1-adrenoceptors in hippocampus  
 of pigs, guinea pigs, calves and humans: regional  
 differences  
 AUTHOR(S): Hoyer, Daniel; Jones, C. Richard; Ford, William;  
 Paliogianni, Jose A.; Pruzin, Sandoz Ltd., Basel, CH-4002, Switz.  
 CORPORATE SOURCE: SOURCE: Eur. J. Pharmacol., Mol. Pharmacol. Sect. (1990),  
 188(1), 9-16  
 CODEN: EJPBMET; ISSN: 0922-4106  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Radioligand binding studies were performed with membranes of  
 guinea pig, pig, calf, and human hippocampus using [<sup>125</sup>I]-labeled BE 2254 (also  
 known as [<sup>125</sup>I]-labeled HEAT as the radioligand. [<sup>125</sup>I]-labeled BE 2254  
 bound with similar high affinity to saturable populations of recognition  
 sites in all 4 membrane preps. Competition curves obtained with a variety  
 of ligands (e.g., WB 4101, benoxathian, 5-methyl-urapidil) were biphasic  
 and the profiles of the high- and low-affinity components of [<sup>125</sup>I]-labeled BE  
 2254 binding were similar in all four membrane preps. The data  
 suggest that [<sup>125</sup>I]-labeled BE 2254 labels 2 subtypes of  
 .alpha.1-adrenoceptors in the hippocampus of these species. [<sup>3</sup>H]WB 4101 was used to label  
 .alpha.1A recognition sites in pig hippocampus membranes. [<sup>3</sup>H]WB 4101  
 recognized with high affinity an apparently homogeneous class of sites, as  
 suggested by monophasic satn. and competition expts. The rank order of  
 affinity of the ligands for the high-affinity component of [<sup>125</sup>I]-labeled BE 2254  
 binding was similar to the rank order of affinity of the drugs for  
 [<sup>3</sup>H]WB 4101 sites. The pharmacol. profile of the low-affinity  
 component of [<sup>125</sup>I]-labeled BE 2254 binding was similar to that described  
 recently for the .alpha.1B-adrenoceptor cloned from DDT1 cells. In autoradiog.  
 studies with human hippocampal slices, CEC (chloroethylclonidine), an  
 alkylating agent described to show selectivity for .alpha.1B-  
 adrenoceptors, displaced preferentially [<sup>125</sup>I]-labeled BE 2254 binding  
 from the mol. layer of the dentate gyrus. In contrast, WB 4101 an  
 .alpha.1A-adrenoceptor-selective ligand, displaced preferentially  
 [<sup>125</sup>I]-labeled BE 2254 binding in the hilus and the CA3 region. The  
 data show that 2 subtypes of .alpha.1-adrenergic recognition sites can be  
 identified in the hippocampus. In the human hippocampus, .alpha.1A  
 sites

L14 ANSWER 197 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 sites are predominant in the hilus and the CA3 region, whereas .alpha.1B sites are predominant in the mol. layer of the dentate gyrus. These subtypes show a similar pharmacol. profile in man, pig, calf and guinea-pig, and may have a different functional role in these two areas of the hippocampus.  
 IT 67339-62-2, ARC 239  
 RL: BIOL (Biological study)  
 (.alpha.1 adrenoceptor subtypes affinity for, of hippocampus of human and lab. animal)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

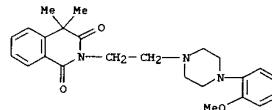


L14 ANSWER 198 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1990:62442 CAPLUS  
 DOCUMENT NUMBER: 112:62442  
 TITLE: Infrared spectroscopy study of interactions affecting tablet disintegration and drug release rate  
 AUTHOR(S): Casahourrat, L.; Pham Van Huong; Larrouture, D.; Heraud, P.; Etienne, A.  
 CORPORATE SOURCE: Inst. Pharm. Ind., Bordeaux, 33000, Fr.  
 SOURCE: Pharm. Acta Helv. (1989), 64(8), 225-30  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 GI



I

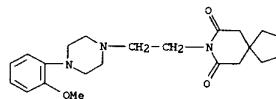
AB IR spectroscopy studies showed that the interaction between the drug (1,3(2H,4H)-Isoquinolinedione (I) and excipients necessary for tablet formulations affected the drug release rate. The interaction was higher at higher compression pressures.  
 IT 55974-42-0  
 RL: PRP (Properties)  
 (interaction of, with excipients, IR spectroscopy study of)  
 RN 55974-42-0 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

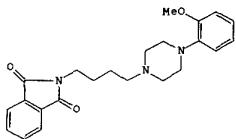
L14 ANSWER 199 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:587459 CAPLUS  
 DOCUMENT NUMBER: 111:187459  
 TITLE: Behavioral studies with anxiolytic drugs. VI. Effects on punished responding of drugs interacting with serotonin receptor subtypes  
 AUTHOR(S): Foust, J.  
 CORPORATE SOURCE: M.J. Barrett, J. E.  
 SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20814-4799, USA  
 DOCUMENT TYPE: J. Pharmacol. Exp. Ther. (1989), 250(3), 809-17  
 LANGUAGE: English  
 AB The effects of drugs that bind selectively to different 5-HT receptor subtypes were assessed in pigeons. Keypecking was maintained by a multiple fixed-ratio schedule of reinforcement in which responding also was punished during one component. The greatest increases in punished responding were produced by the buspirone analogs BMY 7378 and ipsapirone, which act at the 5-HT1A receptor. RU 24969, with high affinity for both 5-HT1 and 5-HT2 receptors, and 1-(2-methoxyphenyl)piperazine, a 5-HT1 compd., increased punished responding to a lesser extent, as did the 5-HT2 antagonists ketanserin and ritanserin. The 5-HT3 antagonists GR 38032F, ICS 205930, and MDL 72222 showed little systematic effect, and the mixed 5-HT1B/5-HT1C compd. 1-(3-chlorophenyl)piperazine decreased punished responding. Levels of neurotransmitter metabolites in cerebrospinal fluid were assessed across a wide dose range of representative drugs used in the behavioral studies. Levels of the 5-HT metabolite 5-HIAA were decreased by BMY 7378 and ipsapirone, were not changed by ritanserin, and were increased at one dose by MDL 72222. Thus, decreased 5-HT neurotransmission is involved in the effects of novel nonbenzodiazepine anxiolytics such as buspirone. The effects of these drugs on other neurotransmitter systems do not play a significant role in their anxiolytic actions.  
 IT 21102-95-4, BMY 7378  
 RL: PRP (Properties)  
 (behavioral anxiolytic effect of, serotonin receptor subtypes in, cerebrospinal fluid monoamine metabolites response to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decan-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 199 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● 2 HCl

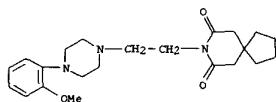
L14 ANSWER 200 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1989:205083 CAPLUS  
 DOCUMENT NUMBER: 110:205083  
 TITLE: Stimulus properties of Arylpiperazines:  
 NAN-190, a potential 5-HT1A serotonin antagonist  
 AUTHOR(S): Glennon, R. A.; Naiman, N. A.; Pierson, M. E.;  
 Titeler, M.; Lyon, R. A.; Herndon, J. L.;  
 Misraheimer,  
 B.  
 CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ.,  
 Richmond, VA, 23298-0591, USA  
 SOURCE: Drug Dev. Res. (1989) 16(2-3-4), 335-43  
 CODEN: DDREDX; ISSN: 0272-4391  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB Arylpiperazines bind both at 5-HT1A and 5-HT1B serotonin receptors. In an attempt to design novel 5-HT1A agonists and antagonists based on the arylpiperazine nucleus, the stimulus properties of a series of such agents were studied in rats trained to discriminate 0.5 mg/kg of the 5-HT1B activity. The agents were modified to eliminate those features and to incorporate structural features important for the 5-HT1A activity. The resulting agents displayed high affinity for 5-HT1A sites. NAN-190 I neither mimicked nor antagonized the TMPP stimulus, but was capable of antagonizing the stimulus produced by the 5-HT1A agonist 8-hydroxy-1-(dipropylamino)tetralin (0.2 mg/kg). NAN-190 may be a potential 5-HT1A antagonist.

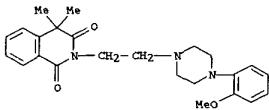
IT 21102-95-4, BMY 7378  
 RL: BIOL (Biological study)  
 (serotonin receptors interaction with, structure in relation to)  
 RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (SCI) (CA INDEX NAME)

L14 ANSWER 200 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



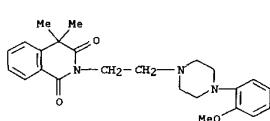
L14 ANSWER 201 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1989:101584 CAPLUS  
 DOCUMENT NUMBER: 110:101584  
 TITLE: Demonstration by infrared spectroscopy of the interactions affecting disintegration time of tablets  
 AUTHOR(S): Casahourrat, L.; Pham V. Huong; Larrouture, D.; Heraud, P.; Etienne, A.  
 CORPORATE SOURCE: Inst. Pharm. Ind., Bordeaux, 33000, Fr.  
 SOURCE: Bull. Tech./Gattefossé Rep. (1987), 80, 33-40  
 CODEN: BTGRDQ  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 AB IR spectroscopy showed that the interaction between a drug [e.g. AR-C 239-2HCl (I)] and various excipients required for tablet formulation affected the disintegration time of tablets, but not the drug dissoln. rate. The excipients used were lactose, corn starch, gelatin, Mg stearate and poly(vinylpyrrolidone). The dissoln. rate of AR-C-HCl was not affected by the compression force, while that of I decreased with an increase in the compression force. The IR method was superior to the DSC method currently used.

IT 55974-42-0 66891-00-1  
 RL: BIOL (Biological study)  
 (tablets, disintegration of and drug release rate from, excipient interactions effect on, IR spectroscopy study of)  
 RN 55974-42-0 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride (SCI) (CA INDEX NAME)

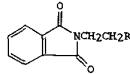


RN 86891-00-1 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride (SCI) (CA INDEX NAME)

L14 ANSWER 201 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1989:18097 CAPLUS  
 DOCUMENT NUMBER: 110:18097  
 TITLE: Antipsychotic properties of new  
 N-(4-substituted-1-piperazinyl-1- and N-(4-substituted-1-piperidinyl-1)-phthalimides  
 AUTHOR(S): Al-Rashood, Khalid A.; Mustafa, Ali A.; Alhaider, Abdulqader; Ginawi, Omer T.; Madani, Abdul Azim  
 E.  
 CORPORATE SOURCE: El-Obeid, Humeida A.  
 Saudi Coll. Pharm., King Saud Univ., Riyadh, 11451,  
 SOURCE: Arabia J. Pharm. Sci. (1988), 77(10), 898-901  
 CODEN: JPMSAE; ISSN: 0022-3549  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

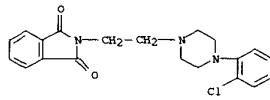


I

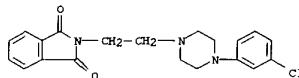
AB A series of N-(4-phenyl- and 4-pyridyl-1-piperazinyl-1- and N-(4-phenyl-1-piperidinyl-1)-phthalimides I (R = 4-aryl-substituted piperazine and piperidine) were synthesized and tested for antipsychotic activity. All compds. suppressed the spontaneous motor activity and the apomorphine-induced climbing in mice and pergolide-induced locomotor activity in rats, demonstrating psychotropic properties equal to the that of sulpiride. Although the compds., like sulpiride, were less potent than haloperidol in blocking the locomotor activities, they caused no catalepsy, a major side effect following treatment with conventional antipsychotic agents. It is likely that the new compds. produce their neuroleptic activities through inhibition of limbic dopamine receptors.

IT 75000-28-1P 75000-29-2P 75000-30-5P  
 117992-67-3P 117992-68-4P 117992-69-5P  
 RL BAC (Biological activity or effector, except adverse); SPN  
 (Synthetic preparation); BIOL (Biological study); PREP (Preparation (prep. and antipsychotic activity of))  
 RN 75000-28-1 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione,  
 Z-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-

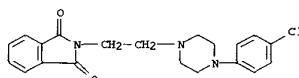
L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (9CI) (CA INDEX NAME)



RN 75000-29-2 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione,  
 Z-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-

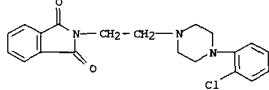


RN 75000-30-5 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione,  
 Z-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-



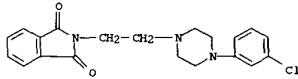
RN 117992-67-3 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione,  
 Z-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



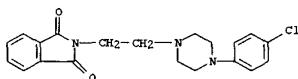
● HCl

RN 117992-68-4 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione,  
 Z-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

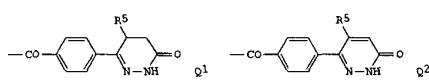
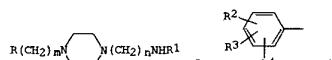
RN 117992-69-5 CAPLUS  
 CN 1H-isindole-1,3(2H)-dione,  
 Z-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L14 ANSWER 203 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1988:590450 CAPLUS  
 DOCUMENT NUMBER: 109:190450  
 Preparation of pyridazinone-containing piperazine derivatives and their salts as cardiotonics  
 INVENTOR(S): Okujima, Hiromi; Narimatsu, Akihiro; Kobayashi, Makio;  
 PATENT ASSIGNEE(S): Furuya, Rikizo; Tsuda, Kunio; Kitada, Yoshi  
 SOURCE: Mitsubishi Kasei Corp., Japan  
 CODEN: JKKXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63154671	A2	19880627	JP 1986-300695	19861217
OTHER SOURCE(S):		MARPAT 109:190450		
GI				



AB Title derivs. I (R = Q; R1 = Q1, Q2; R2 - R4 = H, Cl-5 alkoxy, OH; R5 = H, Cl-5 alkyl; two of R2 - R4 = OCH2, OCH2CH2O; m = 0-4; n = 1-4) and their salts are prep'd. as cardiotonics. A soln. of 1-(4-methoxyphenyl)piperazine and N-(2-bromoethyl)phthalimide in DMF was treated with Et3N at 80.degree. for 5 h and the product (yield 28%) was

stirred with an aq. H2NNH2.H2O in EtOH at 70.degree. for 4 h to give 100 %

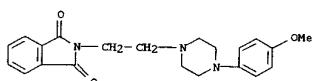
I (R = C6H4OMe-4, R1 = H, m = 0, n = 2) (II).

6-(4-Carboxyphenyl)-2,3,4,5-tetrahydropyridazin-3-one (0.75 g) was treated with ClCO2Et in DMF/THF contg. Et3N between -20 and -30.degree., the reaction mixt. was treated

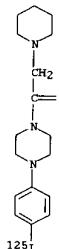
with a soln. of 0.81 g II at -20.degree. for 20 min, and then at room temp. for 2 h to give I (R = C6H4OMe-4, R1 = Q1, R5 = H, m = 0, n = 2) (III), which was treated with aq. HCl/EtOH to give 0.85 g III.HCl (IV).

In guinea pig left atrium in vitro, IV at 10-5 or 3 times. 10-5 g/mL

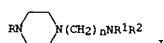
L14 ANSWER 203 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 increased cardiac contractility 42.1 or 58.0%, resp.  
 IT 117046-73-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prep. and redn. of)  
 RN 117046-73-8 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-  
 (9CI) (CA INDEX NAME)



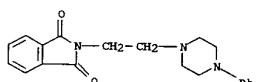
L14 ANSWER 204 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1988:586395 CAPLUS  
 DOCUMENT NUMBER: 109:186395  
 TITLE: The metabolic and kinetic aspects of  
 1-(piperidinoacetyl)-4-(4-iodophenyl)piperazine: a  
 potential brain imaging agent  
 AUTHOR(S): Harirajan, Shankar  
 CORPORATE SOURCE: Northeastern Univ., Boston, MA, USA  
 SOURCE: (1987) 238 pp. Avail.: Univ. Microfilms Int.,  
 Order  
 No. DA8801974  
 From: Diss. Abstr. Int. B 1988, 48(11), 3260  
 DOCUMENT TYPE: Dissertation  
 LANGUAGE: English  
 AB Unavailable  
 IT 117205-94-4, 1-(Piperidinoacetyl)-4-(4-[125I]iodophenyl)piperazine  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (metab. of, brain imaging in relation to)  
 RN 117205-94-4 CAPLUS  
 CN Piperazine, 1-[4-(iodo-125I)phenyl]-4-(1-piperidinylacetyl)- (9CI)  
 (CA INDEX NAME)



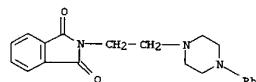
L14 ANSWER 205 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1988:528953 CAPLUS  
 DOCUMENT NUMBER: 109:128953  
 TITLE: Arylpiperazine derivatives as high-affinity  
 5-HT1A  
 serotonin ligands  
 AUTHOR(S): Glennon, Richard A.; Naiman, Noreen A.; Lyon, Robert  
 A.; Tietler, Milt  
 CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298-0581, USA  
 SOURCE: J. Med. Chem. (1988), 31(10), 1968-71  
 CODEN: JMCHEA ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 109:128953  
 GI



AB A small series of 4-substituted 1-arylpiperazines I (R = Ph, 2-MeOC6H4, 1-naphthyl, 2-pyrimidinyl; NR1R2 = phthalimido, NH2, NHAc, NHBz; n = 2-5) was prep'd. in an attempt to develop agents with high affinity for 5-HT1A (5-hydroxytryptamine1A) serotonin binding sites. I (R = Ph, 2-MeOC6H4, 1-naphthyl; NR1R2 = phthalimido, NHBz; n = 4) displayed high affinity for these sites. One of these compds., I (R = 2-MeOC6H4, NR1R2 = phthalimido, n = 4), possessed a higher affinity than 5-HT and represents the highest affinity (Ki = 0.6 nM) agent yet reported for 5-HT1A sites.  
 IT 75000-24-7P 115338-31-3  
 RL: SPP (Synthetic preparation); PREP (Preparation)  
 (prep. and binding affinity of, for hydroxytryptamine receptor site)  
 RN 75000-24-7 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-  
 (9CI) (CA INDEX NAME)



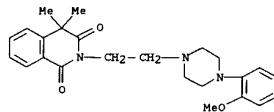
L14 ANSWER 205 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 115338-31-3 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



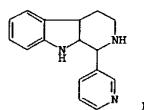
● HCl

L14 ANSWER 206 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1988:417541 CAPLUS  
 DOCUMENT NUMBER: 109:17541  
 TITLE: Alpha-2A and alpha-2B adrenergic receptor  
 subtypes:  
 antagonist binding in tissues and cell lines  
 containing only one subtype  
 AUTHOR(S): Bylund, David B.; Ray-Peterson, Carla; Murphy, T.  
 J.  
 CORPORATE SOURCE: Sch. Med., Univ. Missouri, Columbia, MO, 65212,  
 USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1988), 245(2), 600-7  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The affinities of 34 adrenergic antagonists for .alpha.2-adrenergic receptors were detd. from homogenous radioligand binding studies with [<sup>3</sup>H]yohimbine and [<sup>3</sup>H]rauwolscine. It has been suggested that .alpha.2-adrenergic receptors can be subdivided into .alpha.2A and .alpha.2B subtypes. Oxytetrizoline is selective for .alpha.2A receptors, whereas prazosin is .alpha.2B selective. Five different tissues were used, each of which has only 1 of the 2 subtypes: human platelets (.alpha.2A), the HT29 cell line (.alpha.2A), human cerebral cortex (.alpha.2A), neonatal rat lung (.alpha.2B), and NG108-15 cell line (.alpha.2B). The drug affinities were highly correlated when .alpha.2A tissues were compared with .alpha.2B tissues ( $r = 0.97-0.98$ ) or when the 2 .alpha.2B tissues were compared ( $r = 0.99$ ). By contrast, comparison of an .alpha.2A tissue with an .alpha.2B tissue resulted in poor correlations ( $r = 0.77$  to  $-0.87$ ). Three new subtype-selective drugs were identified among these drugs on the basis of at least a 10-fold greater affinity for 1 subtype. All 3 were selective for the .alpha.2B subtype: ABC-239 (100-fold selective), chlorpromazine (18-fold selective), and 7-hydroxylchlorpromazine (17-fold selective). These studies, by demonstrating distinct pharmacol. profiles for the 2 .alpha.2-adrenergic receptor subtypes in several different tissues, further support the existence and definition of these subtypes. The identification of a cell line for each subtype should be useful in the further study of .alpha.2-adrenergic receptor subtypes.  
 IT 67339-62-2, ABC 239  
 RL: BIOL (Biological study)  
 (as .alpha.2B adrenergic receptor ligand)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 206 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

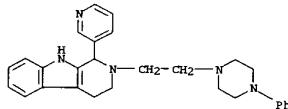


L14 ANSWER 207 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1987-569626 CAPLUS  
 DOCUMENT NUMBER: 107:168626  
 TITLE: Synthesis and pharmacological properties of some 2-substituted 1-(3-pyridyl)-1,2,3,4-tetrahydro-.beta.-carbolines  
 AUTHOR(S): Misztal, Stanislaw; Boksa, Jan;  
 Chojnicka-Wojcik, Ewa;  
 CORPORATE SOURCE: Tarczynska, Ewa; Lewandowska, Anna  
 Inst. Pharmacol., Pol. Acad. Sci., Krakow,  
 31-343,  
 Pol.  
 SOURCE: Pol. J. Pharmacol. Pharm. (1987), 39(1), 97-103  
 CODEN: PJPFAA; ISSN: 0301-0244  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 107:168626  
 GI

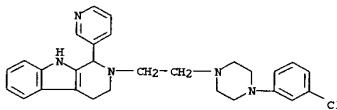


AB The title compds. I ( $R = COCH_2NMe_2$ ,  $(CH_2)_2NMe_2$ ,  $COCH_2$ piperidyl,  $(CH_2)_2$ piperidyl, etc.) were obtained by chloro- or bromoacetylation of 1-(3-pyridyl)-1,2,3,4-tetrahydro-.beta.-carboline followed by reaction with the appropriate amine and LiAlH<sub>4</sub> redn. Some of the compds. showed sedative properties in mice. None possessed neuroleptic, antidepressant, analgesic, or anticonvulsant properties.  
 IT 110785-29-0P 110785-30-3P  
 RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation);  
 BIOL (Biological study); PREP (Preparation)  
 (prep. and neuropharmacol. and toxicity of)  
 RN 110785-29-0 CAPLUS  
 CN 1H-Pyrido[3,4-b]indole, 2,3,4,9-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-1-(3-pyridinyl)- (9CI) (CA INDEX NAME)

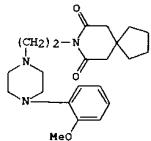
L14 ANSWER 207 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 110785-30-3 CAPLUS  
 CN 1H-Pyrido[3,4-b]indole, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3,4,9-tetrahydro-1-(3-pyridinyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 208 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1987-489746 CAPLUS  
 DOCUMENT NUMBER: 107:09746  
 TITLE: BMY 7378, a buspirone analog with high affinity,  
 selectivity and low intrinsic activity at the  
 5-HT1A  
 membranes  
 AUTHOR(S): Yocca, Frank D.; Hyslop, Deborah K.; Smith,  
 David W.  
 CORPORATE SOURCE: Maayani, Saul  
 Pharm. Res. Dev. Div., Bristol-Myers Co.,  
 Wallingford,  
 CT, 06492-7660, USA  
 SOURCE: Eur. J. Pharmacol. (1987), 137(2-3), 293-4  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

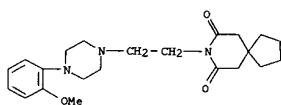


AB The buspirone analog BMY7378 (I) had a high affinity and selectivity for 5-HT1A binding sites in rat and guinea pig hippocampal membrane preps. The drug also had low intrinsic activity.

IT 21102-95-4  
 RL: BIOC (Process)  
 (binding of, to serotonergic S1A receptors of brain)

RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 208 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

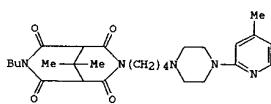
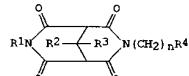
L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1987-156511 CAPLUS  
 DOCUMENT NUMBER: 106:156511  
 TITLE: Preparation of 3,7-diazabicyclo[3.3.1]nonane-2,4,6,8-tetron derivatives as central nervous system agents  
 INVENTOR(S): Schoen, Uwe; Kehrbach, Wolfgang; Benson, Werner;  
 Fuchs, Andreas; Ruhland, Michael  
 PATENT ASSIGNEE(S): Kali-Chemie Pharma G.m.b.H., Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 11 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3529872	A1	19870226	DE 1985-3529872	19850821
ES 556660	A1	19871216	ES 1986-556660	19860625
FI 8603150	A	19870222	FI 1986-3150	19860801
FI 82048	B	19900928		
FI 82048	C	19911110		
EP 212551	A2	19870904	EP 1986-111145	19860812
EP 212551	A3	19860323		
EP 212551	B1	19901024		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 57702	E	19901115	AT 1986-111145	19860812
HU 41788	A2	19870528	HU 1986-3603	19860818
ZU 194233	B	19880128		
ZA 8606243	A	19870429	ZA 1986-6243	19860819
DD 251555	A5	19871118	DD 1986-293732	19860819
US 4771044	A	19880913	US 1986-890843	19860819
NO 8603346	A	19870223	NO 1986-3346	19860820
NO 164901	B	19890820		
NO 164901	C	19890828		
AU 8661619	A1	19870226	AU 1986-61619	19860820
AU 589671	B2	19891019		
DK 8603961	A	19870430	DK 1986-3961	19860820
DK 161648	B	19910729		
DK 161648	C	19920127		
IL 79785	A1	19900712	IL 1986-79785	19860820
CA 1272196	A1	19900731	CA 1986-516366	19860820
JP 62096489	A2	19870502	JP 1986-194120	19860821
JP 07039416	B4	19950501		
ES 557719	A1	19880101	ES 1987-557719	19870915
JP 07267953	A2	19951017	JP 1994-265587	19941028
JP 2525560	B2	19960821		

PRIORITY APPLN. INFO.: DE 1985-3529872 19850821  
 EP 1986-111145 19860812

GI

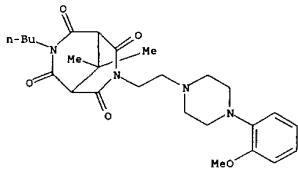
L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



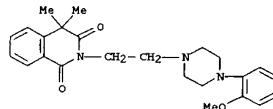
AB The title compds. I [R1 = alkyl, alkenyl, cycloalkylalkyl, phenylalkyl]; R2, R3 = alkyl, Ph; R2R3 = alkylene; R4 = nucleophilic leaving group, (un)substituted 1-piperazinyl; n = 2-10] were prepd. as central nervous system agents (no data). 3-Butyl-9,9-dimethyl-3,7-diazabicyclo[3.3.1]nonane-2,4,6,8-tetron was alkylated with Br(CH<sub>2</sub>)<sub>4</sub>Br to give I (R1 = Bu, R2 = R3 = Me, R4 = Br, n = 4). This was condensed with 1-(4-methyl-2-pyridinyl)piperazine to give diazabicyclononane II. Tablets, each contg. 20 mg II, were prepd. from II 20, cornstarch 30, lactose 55, polyvinylpyrrolidone 5, Mg stearate 2, and hydrogenated castor oil 1 part.

IT 107736-97-0P  
 RL BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Preparation of a central nervous system agent)

RN 107736-97-0 CAPLUS  
 CN 3,7-Diazabicyclo[3.3.1]nonane-2,4,6,8-tetron, 3-butyl-7-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, 9,9-dimethyl- (9CI) (CA INDEX NAME)

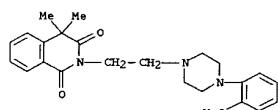


L14 ANSWER 210 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1987:149183 CAPLUS  
 DOCUMENT NUMBER: 106:149183  
 TITLE: The blood pressure effects of alpha-adrenoceptor antagonists injected in the medullary site of action  
 AUTHOR(S): Rousquet, Pascal; Feldman, Josiane  
 CORPORATE SOURCE: Fac. Med., Univ. Louis Pasteur, Strasbourg, 67000, Fr.  
 SOURCE: Life Sci. (1987), 40(11), 1045-52  
 CODEN: LIFSAK; ISSN: 0024-3205  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A series of alpha-blocking drugs were administered to the nucleus reticularis lateralis (NRL) of the medulla oblongata, the main site for the hypotensive action of clonidine, in pentobarbital anesthetized cats. Drugs were injected through a needle which was stereotactically inserted.  
 Prazosin [19216-56-9] (6 nmol) was hypertensive (MBP (mean blood pressure) +25%), corynanthe [483-10-3] had no effect and AR-C239 [67339-62-2], another alpha2-blocker, was hypotensive (MBP -16%). The alpha2-blockers, yohimbine [146-48-5] and idazoxan [79944-58-4] were hypotensive. The blood pressure effects of alpha-blocking drugs directly microinjected in the nucleus reticularis lateralis cannot be simply related to their selectivity for a particular subtype of alpha-receptors.  
 IT 67339-62-2, AR-C239  
 RL: BIOL (Biological study)  
 (blood pressure response to, after injection into nucleus reticularis lateralis, alpha-adrenergic receptor subtypes in)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 211 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1987:96671 CAPLUS  
 DOCUMENT NUMBER: 106:96671  
 TITLE: Alpha-1 adrenergic receptor binding and contraction of rat caudal artery  
 AUTHOR(S): Abel, Peter W.; Minneman, Kenneth P.  
 CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1986), 239(3), 678-86  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Alpha-1 adrenergic receptors were examined in rat caudal artery by using radioligand binding of 125I-labeled BE 2254 [40077-13-2] (125IBE) and in vitro contraction measurements. 125IBE bound rapidly and reversibly to a single class of high-affinity binding sites in membrane preps. of caudal artery. Scatchard anal. gave an equil. dissocon. const. (KD) of 110 pM and d. of binding sites of 115 fmol/mg of protein. Antagonists inhibited 125IBE binding and phenylephrine [59-42-7]-induced contractions competitively, with an order of potency of prazosin [19216-56-9] > AR-C239 [67339-62-2] > phentolamine [50-60-2] > yohimbine [146-48-5]. The pA2 (neg. log of antagonist concn. producing a half-max. effect) values for inhibition of phenylephrine-induced contraction correlated well with KD values for inhibition of specific 125IBE binding. A no. of other full and partial agonists also caused contraction of caudal arteries with an order of potency of epinephrine [51-43-4] > norepinephrine [51-41-2] > phenylephrine > methoxamine [390-28-3]. The order of potency of agonists and the potencies of antagonists suggests that the contractile responses of rat caudal artery were mediated by alpha-1 adrenergic receptors. The 50% effective concn. (EC50) values of partial agonists in causing contraction correlated well with their KD values for inhibition of specific 125IBE binding. However, the EC50 values for full agonists were 30-200-fold lower than their KD values. Treatment of caudal arteries in vitro with 0.1 μM phenoxbenzamine for 10 min to inactivate alpha adrenergic receptors decreased both the potencies of full agonists in causing contraction and the maximal contractile response. Functional equil. dissocon. consts. calc'd. from contraction expts. using phenoxbenzamine agreed well with KD's detd. from binding studies; however, phenoxbenzamine reduced 125IBE binding sites by 50%, whereas the theor. redn. in functional alpha adrenergic receptors averaged

L14 ANSWER 211 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 964. Apparently, 125IBE labels the alpha-1 adrenergic receptors mediating contraction of rat caudal artery. When receptor d. is reduced, the potencies of agonists in activating the receptors agree well with their potencies in binding to the receptors, suggesting that there is a pool of spare alpha-1 adrenergic receptors in this tissue.  
 IT 67339-62-2, AR-C239  
 RL: BIOL (Biological study)  
 (caudal artery contraction by phenylephrine and α.1-adrenergic ligand binding antagonism by)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



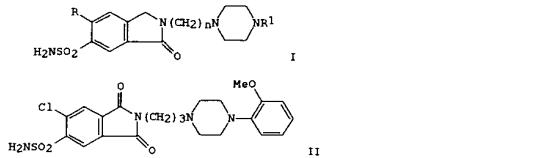
L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1986:424279 CAPLUS  
 DOCUMENT NUMBER: 105:24279  
 TITLE: 2-[1-(Piperazinylalky)-1-oxo-1H-isooindoles  
 INVENTOR(S): Dole, Ferenc H.  
 PATENT ASSIGNEE(S): Bristol-Myers Co., USA  
 SOURCE: Ger. Ofcen. '84 pp.  
 CODEN: GWXXBX

DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3524635	A1	19860123	DE 1985-3524635	19850710
US 4585773	A	19860429	US 1984-629649	19840711
CA 1255311	A1	19890606	CA 1985-485831	19850628
ZA 8505092	A	19860226	ZA 1985-5032	19850705
FI 7802694	A	19860112	FI 1985-2694	19850708
FI 79837	B	19891130		
SE 8503415	A	19860112	SE 1985-3415	19850709
SE 457449	B	19881227		
SE 457449	C	19890420		
ES 545003	A1	19870501	ES 1985-545003	19850709
BE 902847	A1	19860110	BE 1985-215319	19850710
DE 8503150	A	19860112	DK 1985-3150	19850710
DK 163057	B	19892013		
DK 163057	C	19860609		
NO 8502779	A	19860113	NO 1985-2779	19850710
NO 163775	B	19900409		
AU 8544764	A1	19860116	AU 1985-44764	19850710
AU 584104	B2	19890518		
FR 2567519	A1	19860117	FR 1985-10587	19850710
FR 2567519	B1	19900413		
GB 2161807	A1	19860122	GB 1985-17418	19850710
GB 2161807	B2	19871209		
HU 39177	A2	19860828	HU 1985-2669	19850710
HU 195213	B	19880428		
NU 8501998	A	19860203	NL 1985-1998	19850711
JP 040036260	A2	19860220	JP 1985-153333	19850711
JP 040036260	B4	19860106		
AT 8502062	A	19870105	AT 1985-2062	19850711
AT 385270	B	19880310		
CH 664964	A	19880415	CH 1985-3016	19850711
JP 61178364	A2	19860811	JP 1985-271277	198507202
ES 552108	A1	19870801	ES 1986-552108	19860217
NO 8703462	A	19860113	NO 1987-3462	19870817
DK 9100066	A	19910114	DK 1991-66	19910114
PRIORITY APPLN. INFO.:		US 1984-629649		19840711
		NO 1985-2779		19850710

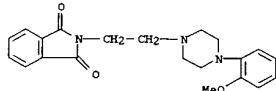
OTHER SOURCE(S): CASREACT 105:24279  
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L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



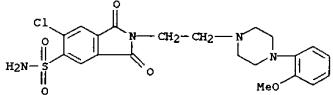
AB The title compds. [I; R = halo, F3C; R1 = (un)substituted Ph, PhCH2, Ez, 2-pyridyl; n = 2-5] were prep'd. as antihypertensives and diuretics. Thus, 1-(2-methoxyphenyl)piperazine was quant. condensed with N-(3-bromopropyl)phthalimide and the product deprotected with NH4 to give 95% 1-(3-aminopropyl)-4-(2-methoxyphenyl)piperazine. This was condensed with 4-chloro-5-sulfamoylphthalimide to give 61% (piperazinylpropyl)phthalimide II which was selectively reduced with Zn in HOAc to give 77% I (R = Cl, R1 = 2-MeOC6H4) (III). In rats 30 mg III/kg reduced blood pressure 84 mmHg.

IT 99718-67-9  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. and hydrazinolysis of)  
 RN 99718-67-9 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(2-methoxyphenyl)-1-piperazinyl]ethyl]-  
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-1,3-dioxo- (SCI) (CA INDEX NAME)

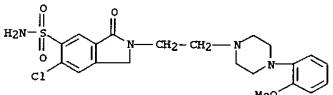


IT 102391-88-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. and redn. of)  
 RN 102391-88-8 CAPLUS  
 CN 1H-Isoindole-5-sulfonamide,  
 6-chloro-2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-  
 1-piperazinyl]ethyl]-3-oxo- (SCI) (CA INDEX NAME)

L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 102391-72-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. of, as antihypertensive and diuretic)  
 RN 102391-72-0 CAPLUS  
 CN 1H-Isoindole-5-sulfonamide,  
 6-chloro-2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-  
 1-piperazinyl]ethyl]-3-oxo- (SCI) (CA INDEX NAME)



L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1986:141729 CAPLUS  
 DOCUMENT NUMBER: 104:141729  
 TITLE: Antivertigo agents. V. Quantitative structure-activity relationships of

6-[2-(4-aryl-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-

1,6-naphthyridines

AUTHOR(S): Shiozawa, Akira; Kogo, Yoshiya; Ichikawa,

Komuro, Chikara; Ishikawa, Michio; Kurashige,

Miyazaki, Hiroshi; Yamanaka, Hiroshi; Sakamoto,

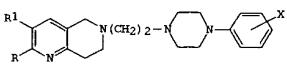
Takao CORPORATE SOURCE: Res. Lab., Nippon Kayaku Co., Tokyo, 115, Japan

SOURCE: Chem. Pharm. Bull. (1985), 33(12), 5332-40

DOCUMENT TYPE: CFBTAL; ISSN: 0009-2363

LANGUAGE: English

GI



AB The quant. structure-activity relationships (QSAR) between the mol. structures and antivertigo activities of

6-[2-(4-arylpiperazinyl)ethyl]-5,6,7,8-tetrahydro-1,6-naphthyridines I (R1R2 = (CH2)4; R1 = R2 = H;

X = H, F, Cl, Me, NM2, OMe, OEt, SME, etc.) were investigated. The effects of

the ortho-, meta-, and para-substituents on the Ph ring of the arylpiperazine moiety were exmd. by means of regression anal. using various physicochem. parameters related to these substituents. The results showed that only the parameters concerning the ortho-substituent

were statistically significant. Namely, the relative activity depended on both Forstho (Swain-Lupton field effect const. of the

ortho-substituent)

and I (indicator variable for the presence of an o-alkoxy group and an o-dimethylamino group). Thus, regression anal. for only the ortho-substituted compds. was exmd. and afforded a result similar to that

described above. Further, the net at. charge calcd. by the MO method besides free energy-related substituent parameters was used as electronic parameters of the ortho-substituents on the Ph ring for this QSAR anal.

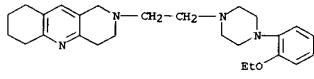
For the ortho-substituted compds. alone, the potency correlated well with

L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (Qortho),  
 while the correlation for all the compds. (ortho-, meta-, and para-substituted) was slightly lower than that for the ortho-substituted compds. alone. It was found that increase in the neg. net at. charge on the first atom of the ortho-position increased the relative activity. The correlation between Qortho, and Fortho and I was exmd. and the role of I is discussed in connection with H bond-forming ability. The interaction between the arylpiperazine moiety in the compd. and a putative receptor is discussed based on the QSAR anal.

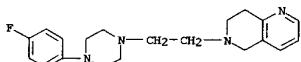
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 83082-27-3 83082-29-5 83082-65-9  
 83100-19-0 83100-22-5 83100-24-7  
 83100-35-0 95355-89-8 95355-91-2  
 95355-93-4 95355-95-6 95355-97-8  
 95355-99-0 95356-01-7 95356-06-2  
 95356-07-3 95356-08-4 95356-09-5  
 95356-10-8 95356-11-9 95356-12-0  
 95356-13-1 95356-14-2

RL: BA (Biological activity or effector, except adverse); BIOL (Biological study)  
 (antivertigo activity of, structure in relation to)

RN 03081-77-0 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine,  
 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



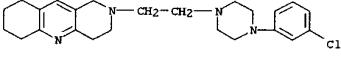
RN 83082-17-1 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(4-fluorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



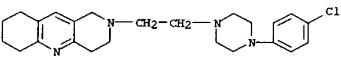
RN 83082-23-9 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine,  
 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-

L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

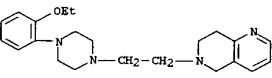
RN 83100-22-5 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine,  
 2-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



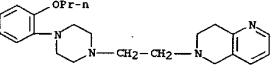
RN 83100-24-7 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine,  
 2-[2-(4-(4-chlorophenyl)-1-piperazinyl)ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-35-0 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

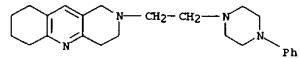


RN 95355-89-8 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-propoxyphe-  
 nyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

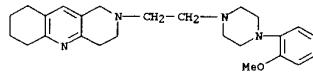


RN 95355-91-2 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(2-butoxyphe- nyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

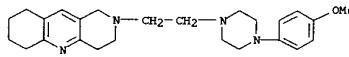
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



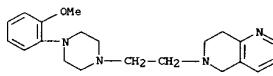
RN 83082-27-3 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



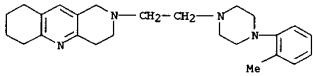
RN 83082-29-5 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



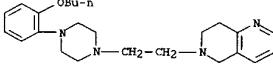
RN 83082-65-9 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



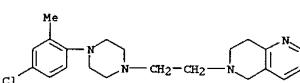
RN 83100-19-0 CAPLUS  
 CN Benzo[b] [1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



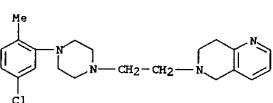
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



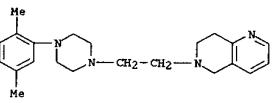
RN 95355-93-4 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(4-chloro-2-methylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



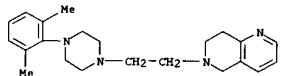
RN 95355-95-6 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(5-chloro-2-methylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



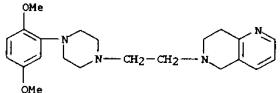
RN 95355-97-8 CAPLUS  
 CN 1,6-Naphthyridine, 6-[2-(4-(2,5-dimethylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



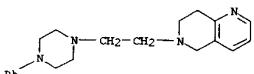
RN 95355-99-0 CAPLUS  
 CN 1,6-Naphthyridine, 6-[2-(4-(2,6-dimethylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



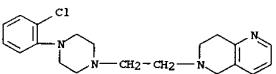
RN 95356-01-7 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



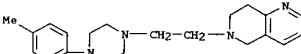
RN 95356-06-2 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



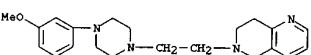
RN 95356-07-3 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



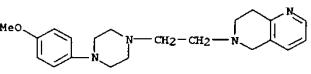
RN 95356-08-4 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



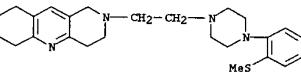
RN 95356-13-1 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



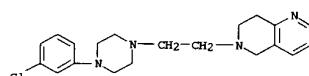
RN 95356-14-2 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



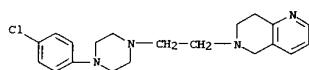
IT 89009-91-6P 101413-03-OP 101413-04-1P  
101413-05-2P 101413-06-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. and antivertigo activity of, structure in relation to)  
RN 89009-91-6 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-[2-(methylthio)phenyl]-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



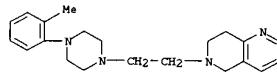
RN 101413-03-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-(4-(2-fluorophenyl)-1-piperazinyl)ethyl]-  
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



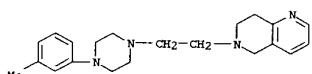
RN 95356-09-5 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



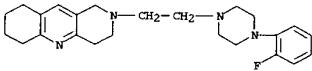
RN 95356-10-8 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



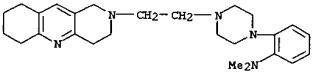
RN 95356-11-9 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



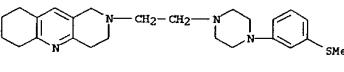
RN 95356-12-0 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



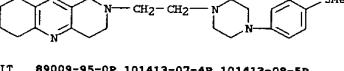
RN 101413-04-1 CAPLUS  
CN Benzenamine,  
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 101413-05-2 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(3-methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

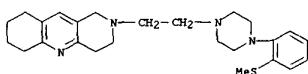


RN 101413-06-3 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



IT 89009-95-0P 101413-07-4P 101413-08-5P  
101413-09-6P 101413-10-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)  
RN 89009-95-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-(methylthio)phenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)  
(9CI) (CA INDEX NAME)

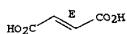
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CRN 89009-91-6  
 CMF C25 H34 N4 S



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

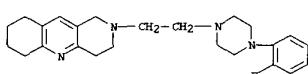
Double bond geometry as shown.



RN 101413-07-4 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-  
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

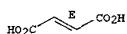
CRN 101413-03-0  
 CMF C24 H31 F N4



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.

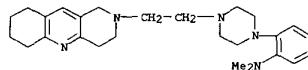


L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 101413-08-5 CAPLUS  
 CN Benzenamine,  
 2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-  
 yl)ethyl]-1-piperazinyl]-N,N-dimethyl-, (2E)-2-butenedioate (1:2)  
 (9CI) (CA INDEX NAME)

CM 1

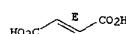
CRN 101413-04-1  
 CMF C26 H37 NS



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

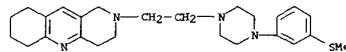
Double bond geometry as shown.



RN 101413-09-6 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(3-  
 (methylthio)phenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)  
 (9CI) (CA INDEX NAME)

CM 1

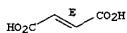
CRN 101413-05-2  
 CMF C25 H34 N4 S



CM 2

L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

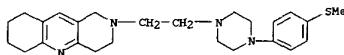
Double bond geometry as shown.



RN 101413-10-9 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(  
 (methylthio)phenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)  
 (9CI) (CA INDEX NAME)

CM 1

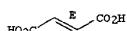
CRN 101413-06-3  
 CMF C25 H34 N4 S



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



L14 ANSWER 214 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:61789 CAPLUS

DOCUMENT NUMBER: 104:61789

TITLE: Further investigations on the

.alpha.1-adrenoceptor

AUTHOR(S): blocking properties of AR-C 239 in rats  
 Huchet, Anne Marie; Andrejak, Michel; Lucet,  
 Bernadette; Gautret, Bruno; Doursout, Marie

Francoise;

CORPORATE SOURCE: Ostermann, Gerard; Schmitt, Henri  
 75006, Dep. Pharmacol., Fac. Med. Broussais, Paris,

SOURCE: Fr.

505-13 Clin. Exp. Pharmacol. Physiol. (1985), 12(5),  
 CODEN: CEXPB9; ISSN: 0305-1870

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB AR-C 239 [67339-62-2], an .alpha.-adrenoceptor-blocking drug,  
 appears to act selectively on .alpha.1 sites in rats. At peripheral  
 sites, this drug did not change the tachycardia induced by spinal  
 sympathetic outflow stimulation in pithed rats, and did not  
 antagonize the inhibitory effects of clonidine on this prepn. In addn., AR-C 239  
 showed predominant .alpha.1-adrenoceptor-blocking properties in the bisected  
 rat

vas deferens prepn. AR-C 239 did not prevent or reverse the centrally  
 mediated hypotensive and bradycardic actions induced by clonidine, in  
 intact animals. Thus, AR-C 239 seems to be a very useful tool for the  
 characterization of peripheral and central .alpha.1-adrenoceptors, in  
 this

animal species.

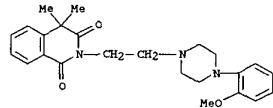
IT 67339-62-2

RL: BIOL (Biological study)

(as .alpha.1-sympatholytic)

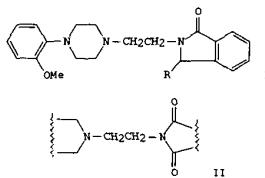
RN 67339-62-2 CAPLUS

CN 1,3(2H,4H)-Isoquinolinodiones, 2-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



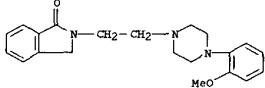
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1986:34108 CAPLUS  
 DOCUMENT NUMBER: 104:34108  
 TITLE: 2-Methoxyphenylpiperazine derivatives.  
 INVENTOR(S): Nagano, Hiroyuki; Takagi, Michiro; Kubodera, Noboru;  
 Matsunaga, Isao; Nahata, Hiroyuki; Oba, Yasuhiro; Sakai, Kazunari; Uchida, Yasuyoshi  
 PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 2 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60169461	A2	19850902	JP 1984-24074	19840210
JP 03053301	B4	19910814	CASREACT 104:34108	GI

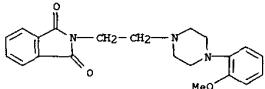


AB Title compds. I ( $R = H, OH$ ) and their salts, useful as cardiovascular agents (no data), were prep'd. Thus, stirring 2.88 g II and 800 mg NaBH<sub>4</sub> in MeOH at room temp. for 5 h gave 2.3 g I ( $R = OH$ ).  
 IT 99718-68-0P 99718-69-1P 99718-70-4P  
 99718-71-5P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prep'n of, as cardiovascular agent)  
 RN 99718-68-0 CAPLUS  
 CN 1H-Indolinol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

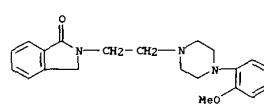
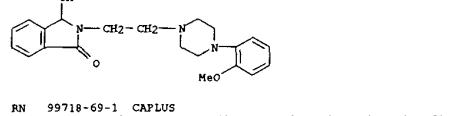
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



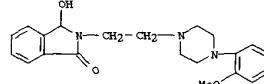
IT 99718-67-9  
 RL: RCT (Reactant)  
 (redn. of, with sodium borohydride)  
 RN 99718-67-9 CAPLUS  
 CN 1H-Indole-1,3(2H)-dione,  
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 99718-70-4 CAPLUS  
 CN 1H-Indolinol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



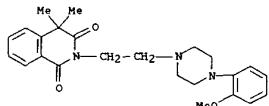
•x HCl

RN 99718-71-5 CAPLUS  
 CN 1H-Indolinol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

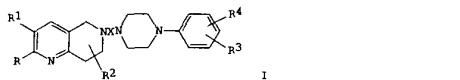
L14 ANSWER 216 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1985:499213 CAPLUS  
 DOCUMENT NUMBER: 103:499213  
 TITLE: [<sup>3</sup>H]-Rauwolscine binding to .alpha.2-adrenoceptors in the mammalian kidney: apparent receptor heterogeneity

between species  
 AUTHOR(S): Neylon, C. B.; Summers, R. J.  
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Melbourne, Parkville, 3052, Australia  
 SOURCE: Br. J. Pharmacol. (1985), 85(2), 349-59  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Binding of the .alpha.2-adrenoceptor antagonist <sup>3</sup>H-labeled rauwolscine [<sup>3</sup>H-103] was characterized in membrane preps. from the kidneys of mouse, rat, rabbit, dog, and man. In all species, binding reached equil. within 45 min and dissociated at a single exponential rate after addn. of phenolamine 10  $\mu$ M. Satn. studies showed that the affinity of [<sup>3</sup>H]rauwolscine was similar in all species (2.33-3.03 nM) except man where it was higher (0.98 nM). Marked differences were seen in the d. of binding sites, increasing in the order: man < dog < rabbit < rat < mouse. In all cases, Hill coeffs. were not different from unity. [<sup>3</sup>H]rauwolscine binds with low affinity (dissocn. const.  $K_D > 15$  nM) to membranes prep'd. from guinea-pig kidney. The low affinity binding is not due to the absence of particular ions in the incubation medium or to receptor occupation by endogenous agonist. The binding in all species was stereoselective with respect to the isomers of noradrenaline. However, differences were seen in the characteristics of agonist interactions with the binding site both between isomers and between species. Marked differences in affinity of particular .alpha.-adrenoceptor antagonists were obsd. for .alpha.2-adrenoceptors labeled by [<sup>3</sup>H]rauwolscine. These differences were most evident with the .alpha.1-adrenoceptor selective antagonist prazosin [19216-56-9] which displayed inhibition consts. ( $K_I$  values) of 33.2, 39.5, 261, 570, and 595 nM in rat, mouse, dog, man, and rabbit, resp. Differences are apparent in the characteristics of .alpha.2-adrenoceptors labeled by [<sup>3</sup>H]rauwolscine between species and the differences obsd. for .alpha.1-selective antagonists such as prazosin may be related to binding to addnl. sites in the vicinity of the .alpha.2-adrenoceptor.  
 IT 67339-62-2  
 RL: BIOL (Biological study)  
 (.alpha.2-adrenoceptor binding of, in kidney of human and lab. animals,

L14 ANSWER 216 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 species variations in)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolininedione, 2-(2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl)-4,4-dimethyl- (9CI) (CA INDEX NAME)



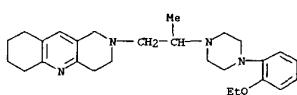
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACESSION NUMBER: 1985:149226 CAPLUS  
 DOCUMENT NUMBER: 102:149226  
 TITLE: Antivertigo agents. IV. Synthesis and  
 antivertigo  
 activity of  
 6-[omega-(4-aryl-1-piperazinyl)alkyl]-  
 5,6,7,8-tetrahydro-1,6-naphthyridines  
 AUTHOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Komuro,  
 Chikara;  
 Ishikawa, Michio; Furuta, Yasuhiko; Kurashige,  
 Shuji;  
 Miyazaki, Hiroshi; Yamada, Hiroshi; Sakamoto,  
 Takao  
 CORPORATE SOURCE: Res. Lab. Pharm. Div., Nippon Kayaku Co., Tokyo,  
 115,  
 Japan  
 SOURCE: Chem. Pharm. Bull. (1984), 32(10), 3981-93  
 CODEN: CPBTAL; ISSN: 0009-2363  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



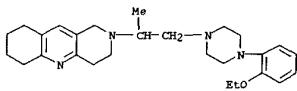
AB 6-[omega-(4-Aryl-1-piperazinyl)alkyl]-5,6,7,8-tetrahydro-1,6-naphthyridines I [R, R1 = H, Me; RRI = (CH2)4; R2 = H, 5-Me 7-Me, 8-Me; R3 = H, F, Cl, Me, alkoxy; R4 = H, Cl; Me, OMe; X = alkylene] (50 compds.) were synthesized and evaluated for antivertigo activity by testing their ability to inhibit spontaneous nystagmus in cats. Structure-activity relationships are discussed. Many I having the 4-(2-alkoxymethyl)piperazine group showed more potent antivertigo activity than diphenidol. Among them, I (RRI = (CH2)4, R2 = R4 = H, R3 = 2-EtO, X = CH2CH2) was selected as a promising antivertigo agent. This compd. also exhibited a more potent inhibitory effect on apomorphine-induced vomiting in dogs than diphenidol.  
 IT 83081-59-8P 83081-71-4P 83081-72-5P  
 83081-73-6P 83081-76-9P 83081-77-0P  
 83081-78-1P 83082-17-1P 83082-18-2P  
 83082-23-9P 83082-24-0P 83082-27-3P  
 83082-28-4P 83082-29-5P 83082-30-6P  
 83082-37-5P 83082-38-6P 83082-59-1P  
 83082-61-5P 83082-62-6P 83082-65-9P

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

83082-67-1P 83100-13-4P 83100-14-5P  
 83100-17-8P 83100-18-9P 83100-19-0P  
 83100-20-3P 83100-22-5P 83100-23-6P  
 83100-24-7P 83100-25-8P 83100-35-0P  
 83100-36-1P 84328-17-6P 95355-09-0P  
 95355-90-1P 95355-91-2P 95355-92-3P  
 95355-93-4P 95355-94-5P 95355-95-6P  
 95355-96-7P 95355-97-8P 95355-98-9P  
 95355-99-0P 95356-00-6P 95356-01-7P  
 95356-02-8P 95356-03-9P 95356-04-0P  
 95356-05-1P 95356-06-2P 95356-07-3P  
 95356-08-4P 95356-09-5P 95356-10-6P  
 95356-11-9P 95356-12-0P 95356-13-1P  
 95356-14-2P 95356-61-2P 95356-62-3P  
 95356-63-4P 95356-64-5P 95356-65-6P  
 95395-66-7P 95395-67-8P 95395-68-9P  
 95410-22-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepns. and antivertigo activity of)  
 RN 83081-59-8 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)propyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



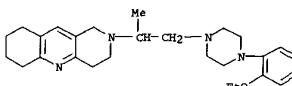
RN 83081-71-4 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)-1-methylethyl]-1-,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83081-72-5 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)-1-methylethyl]-1-,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2)  
 (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1  
 CRN 83081-71-4  
 CMF C27 H38 N4 O



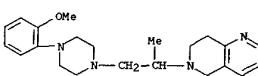
CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



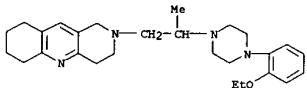
RN 83081-73-6 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methoxyphenyl)-1-piperazinyl)-1-methylethyl]- (9CI) (CA INDEX NAME)



RN 83081-76-9 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)propyl]-  
 1,2,3,4,6,7,8,9-octahydro-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2)  
 (9CI) (CA INDEX NAME)

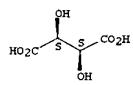
CM 1

CRN 83081-59-8  
 CMF C27 H38 N4 O

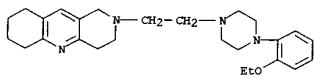


CH 2  
CRN 133-37-9  
CMF C4 H6 O6

Relative stereochemistry.

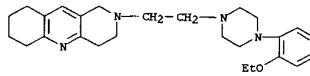


RN 83081-77-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-  
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



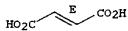
RN 83081-78-1 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-  
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1  
CRN 83081-77-0  
CMF C26 H36 N4 O

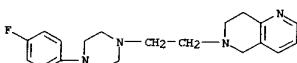


CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

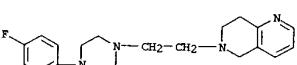


RN 83082-17-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-  
tetrahydro- (9CI) (CA INDEX NAME)



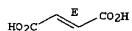
RN 83082-18-2 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-  
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1  
CRN 83082-17-1  
CMF C20 H25 F N4

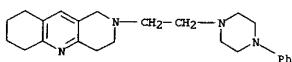


CH 2  
CRN 110-17-8

Double bond geometry as shown.

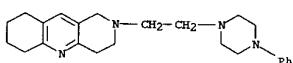


RN 83082-23-9 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-  
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



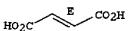
RN 83082-24-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-  
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1  
CRN 83082-23-9  
CMF C24 H32 N4

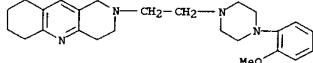


CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

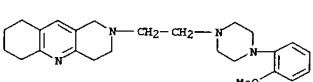


RN 83082-27-3 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(2-  
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



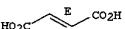
RN 83082-28-4 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(2-  
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)  
(CA INDEX NAME)

CH 1  
CRN 83082-27-3  
CMF C25 H34 N4 O

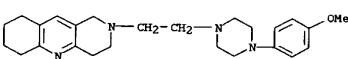


CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

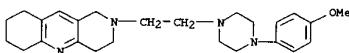


RN 83082-29-5 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-  
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-  
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)  
(CA INDEX NAME)

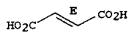
CRN 83082-29-5  
CMF C25 H34 N4 O



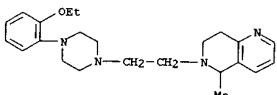
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



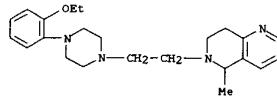
RN 83082-37-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-5-methyl- (9CI) (CA INDEX NAME)



RN 83082-38-6 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-5-methyl-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI)  
(CA INDEX NAME)

CM 1

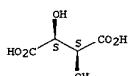
CRN 83082-37-5  
CMF C23 H32 N4 O



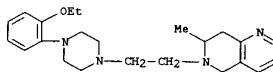
CM 2

CRN 133-37-9  
CMF C4 H6 O6

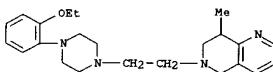
Relative stereochemistry.



RN 83082-59-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



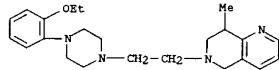
RN 83082-61-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 83082-62-6 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

CM 1

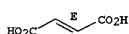
CRN 83082-61-5  
CMF C23 H32 N4 O



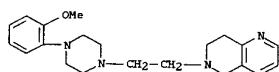
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



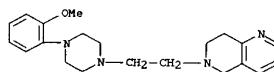
RN 83082-65-9 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-67-1 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

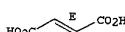
CRN 83082-65-9  
CMF C21 H28 N4 O



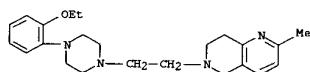
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



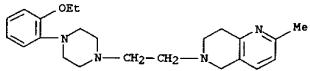
RN 83100-13-4 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 83100-14-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-13-4  
CMF C23 H32 N4 O



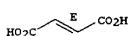
CM 2

CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

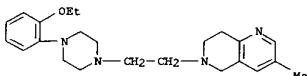
CN Benzo[b] [1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[4-(2-methylphenyl)-1-piperazinyl]ethyl - (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 83100-17-8 CAPLUS

CN 1,6-Naphthyridine, 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



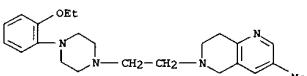
RN 83100-18-9 CAPLUS

CN 1,6-Naphthyridine, 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-17-8

CMF C23 H32 N4 O



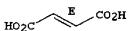
CM 2

CRN 110-17-8

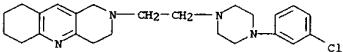
CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.



L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



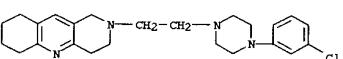
RN 83100-23-6 CAPLUS

CN Benzo[b] [1,6]naphthyridine, 2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl - 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-22-5

CMF C24 H31 Cl N4



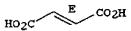
CM 2

CRN 110-17-8

CMF C4 H4 O4

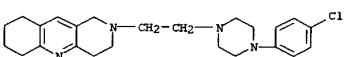
CDES 2:E

Double bond geometry as shown.



RN 83100-24-7 CAPLUS

CN Benzo[b] [1,6]naphthyridine, 2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl - 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



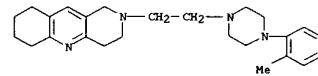
RN 83100-25-8 CAPLUS

CN Benzo[b] [1,6]naphthyridine, 2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl - 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 83100-19-0 CAPLUS

CN Benzo[b] [1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl] - (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS

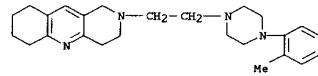
CN Benzo[b] [1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl] - (2E)-2-butenedioate (1:2) (9CI)

(CA INDEX NAME)

CM 1

CRN 83100-19-0

CMF C25 H34 N4



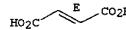
CM 2

CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.



RN 83100-22-5 CAPLUS

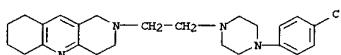
CN Benzo[b] [1,6]naphthyridine, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl] - 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

CRN 83100-24-7

CMF C24 H31 Cl N4



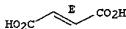
CM 2

CRN 110-17-8

CMF C4 H4 O4

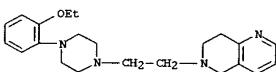
CDES 2:E

Double bond geometry as shown.



RN 83100-35-0 CAPLUS

CN 1,6-Naphthyridine, 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl] - 5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



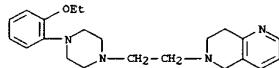
RN 83100-36-1 CAPLUS

CN 1,6-Naphthyridine, 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl] - 5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-35-0

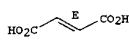
CMF C22 H30 N4 O



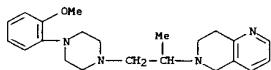
CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

RN 84328-17-6 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methyllethyl]-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

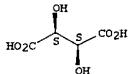
CM 1

CRN 83081-73-6  
CNF C22 H30 N4 O

CM 2

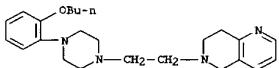
CRN 133-37-9  
CNF C4 H6 O6

Relative stereochemistry.



RN 95355-89-8 CAPLUS

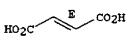
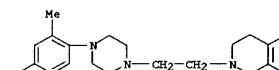
CM 1

CRN 95355-91-2  
CNF C24 H34 N4 O

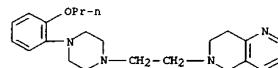
CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

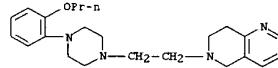
Double bond geometry as shown.

RN 95355-93-4 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(4-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)RN 95355-94-5 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(4-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-93-4  
CNF C21 H27 Cl N4RN 95355-90-1 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-propoxypyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

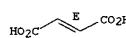
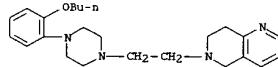
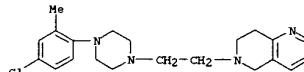
CM 1

CRN 95355-89-8  
CNF C23 H32 N4 O

CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

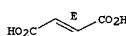
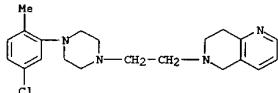
Double bond geometry as shown.

RN 95355-91-2 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2-butoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)RN 95355-92-3 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2-butoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

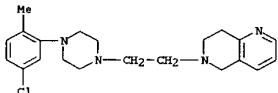
CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

RN 95355-95-6 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)RN 95355-96-7 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

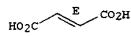
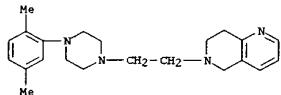
CM 1

CRN 95355-95-6  
CNF C21 H27 Cl N4

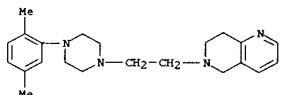
CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

RN 95355-97-8 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)RN 95355-98-9 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

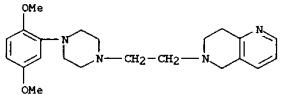
CM 1

CRN 95355-97-8  
CNF C22 H30 N4

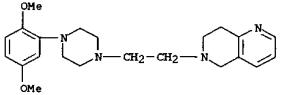
CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

RN 95356-02-8 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

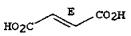
CM 1

CRN 95356-01-7  
CNF C22 H30 N4 O2

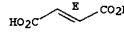
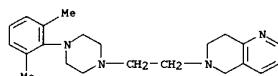
CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

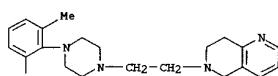
Double bond geometry as shown.

RN 95356-03-9 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83082-59-1  
CNF C23 H32 N4 ORN 95355-99-0 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)RN 95356-00-6 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

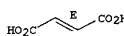
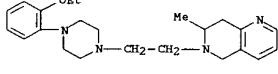
CM 1

CRN 95355-99-0  
CNF C22 H30 N4

CM 2

CRN 110-17-8  
CNF C4 H4 O4  
CDES 2:E

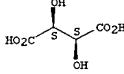
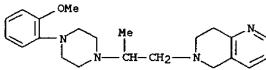
Double bond geometry as shown.

RN 95356-01-7 CAPLUS  
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

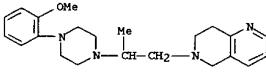
CM 2

CRN 133-37-9  
CNF C4 H6 O6

Relative stereochemistry.

RN 95356-04-0 CAPLUS  
CN 1,6-Naphthyridine, 6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)RN 95356-05-1 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

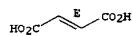
CRN 95356-04-0  
CNF C22 H30 N4 O

CM 2

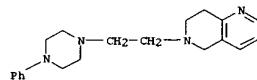
CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CMF C4 H4 O4  
 CDES 2:E

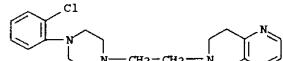
Double bond geometry as shown.



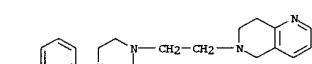
RN 95356-06-2 CAPLUS  
 CN 1,6-Naphthyridine,  
 5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-  
 (9CI) (CA INDEX NAME)



RN 95356-07-3 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
 tetrahydro- (9CI) (CA INDEX NAME)



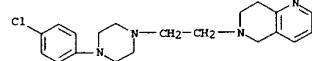
RN 95356-08-4 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
 tetrahydro- (9CI) (CA INDEX NAME)



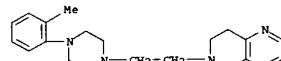
RN 95356-09-5 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(4-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
 tetrahydro- (9CI) (CA INDEX NAME)

RN 95356-10-8 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

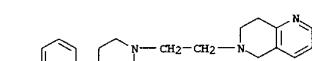
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



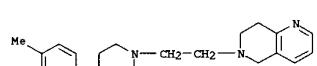
RN 95356-11-9 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(3-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 95356-12-0 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(4-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

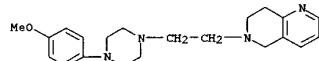


RN 95356-13-1 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(3-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 95356-14-2 CAPLUS

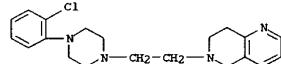
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 95395-61-2 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

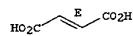
CRN 95356-07-3  
 CMF C20 H25 Cl N4



CH 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.

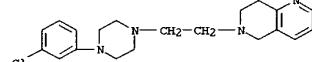


RN 95395-62-3 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-08-4  
 CMF C20 H25 Cl N4

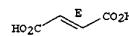
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

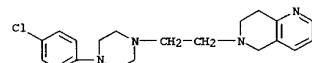
Double bond geometry as shown.



RN 95395-63-4 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-(4-(4-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

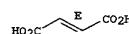
CRN 95356-09-5  
 CMF C20 H25 Cl N4



CH 2

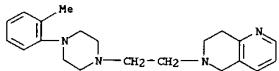
CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



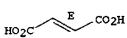
RN 95395-64-5 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

**CM** 1  
CRN 95356-10-8  
CMF C21 H28 N4



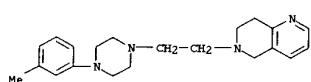
**CM** 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 95395-65-6 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

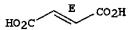
**CM** 1  
CRN 95356-11-9  
CMF C21 H28 N4



**CM** 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

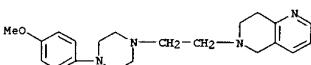
Double bond geometry as shown.

Double bond geometry as shown.



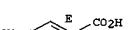
RN 95395-68-9 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

**CM** 1  
CRN 95356-14-2  
CMF C21 H28 N4



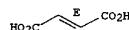
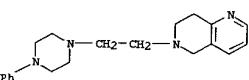
**CM** 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



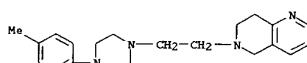
RN 95410-22-3 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

**CM** 1  
CRN 95356-06-2  
CMF C20 H26 N4



RN 95395-66-7 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

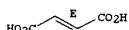
**CM** 1  
CRN 95356-12-0  
CMF C21 H28 N4



**CM** 2

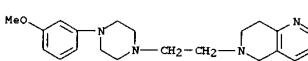
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 95395-67-8 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

**CM** 1  
CRN 95356-13-1  
CMF C21 H28 N4 O



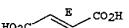
**CM** 2

CRN 110-17-8  
CMF C4 H4 O4

**CM** 2

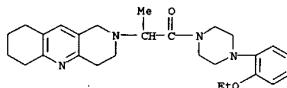
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



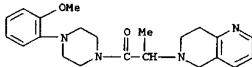
IT 83099-95-0P 95395-47-4P  
RL RCT (Reactant); SPW (Synthetic preparation); PREP (Preparation)  
(prepns. and reacn. of)

RN 83099-95-0 CAPLUS  
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)



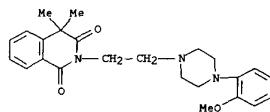
RN 95395-47-4 CAPLUS

CN Piperazine,  
1-[2-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-1-oxopropyl]-4-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

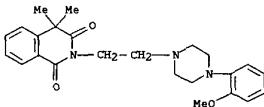


L14 ANSWER 218 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1985:73242 CAPLUS  
 DOCUMENT NUMBER: 102:73242  
 TITLE: Calcium influx-dependent and -independent .alpha.1-adrenoceptor-mediated processes of vasoconstriction in vivo do not operate via different .alpha.1-adrenoceptor subtypes  
 AUTHOR(S): Korstanje, Cornelis; Wilfert, Bob; De Jonge, Adriana; Thoelen, Martin J. M. C.; Timmermans, Pieter B.  
 M. W.  
 CORPORATE SOURCE: M. J. Van Zwieten, Pieter A.  
 Dep. Pharm., Univ. Amsterdam, Amsterdam, 1018 TV, Neth.  
 SOURCE: J. Cardiovasc. Pharmacol. (1984), 6(6), 1102-8  
 CODEN: JCPCDT; ISSN: 0160-2446  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In pithed rats, the selective .alpha.1-adrenoceptor agonists St 587 [15327-38-5] and cirazoline [59939-16-1] show preponderant Ca influx-dependent and -independent vasoconstriction, resp. Using these agonists, selective (competitive) antagonists for either process of vasoconstriction were sought. For this purpose, antagonism was analyzed for 8 structurally different antagonists (prazosin [19216-56-9], BE 2254 [40077-13-2], AR-C239 [67339-62-2], R 28935 [55806-43-4], corynanthine [483-10-3], phenolamine [50-60-2], sulpiride [15676-16-1], and chlorpromazine [50-53-3]) opposing the pressor responses evoked by cirazoline and St 587. Where pA<sub>2</sub> values (-log dose) antagonist evoking a 2-fold shift for the agonist dose-response curve could be calcd., no significantly different pA<sub>2</sub> values against either agonist resulted. However, with respect to the slopes of the Schild plots, deviations from 1 were found for prazosin, R 28935, AR-C239, sulpiride, and chlorpromazine, but not uniformly against both agonists. Following treatment with phenoxybenzamine (PB) (30 .mu.g/kg) and nifedipine (1 mg/kg), which produced Ca influx-sensitive and -insensitive vasoconstriction to cirazoline, resp., Schild plots were constructed for BE 2254, prazosin, and chlorpromazine. Using cirazoline as an agonist, unity slopes were now obtained for prazosin and chlorpromazine. The Schild plots of BE 2254 vs. cirazoline after PB or nifedipine administration, however, exhibited a slope deviating from 1. For prazosin and chlorpromazine, identical pA<sub>2</sub> values still resulted against both processes of vasoconstriction to cirazoline. Evidently, .alpha.1-adrenoceptors Ca influx-dependent and -independent vasoconstriction in vivo are not distinctly different entities, but are sep. recognition sites of the same receptor.

L14 ANSWER 218 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 IT 67339-62-2  
 RI: BIOL (Biological study)  
 (blood vessel contraction inhibition by, adrenergic receptors and calcium in relation to)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isoquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

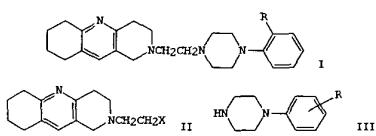


L14 ANSWER 219 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1984:604190 CAPLUS  
 DOCUMENT NUMBER: 101:204190  
 TITLE: Non-specific, time-dependent desensitization of the vas deferens and anococcygeus preparations of the rat to .alpha.1-adrenoceptor antagonists and atropine  
 AUTHOR(S): Onnen, Igor  
 CORPORATE SOURCE: Fac. Med., Univ. Paris-Nord, Bobigny, Fr.  
 SOURCE: Br. J. Pharmacol. (1984), 83(1), 7-14  
 CODEN: BJPCBM; ISSN: 0007-1188  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Rat vas deferens prepns. became desensitized to the .alpha.1-adrenoceptor antagonist thymoxamine [54-32-0]: after 6 h in vitro, the 4 value (time to attain half the occupancy of receptors occupied at equil.) of the response to this drug was 1.50 fold greater in control strips (strips exposed to thymoxamine at 6 h) than in test strips (strips exposed to thymoxamine at 1 h). The rate of action of the .alpha.1-adrenoceptor antagonist AR-C239 [67339-62-2] on the rat anococcygeus prepn. was correlated with the rate of action of atropine [51-55-8]. There was also a significant correlation between the 4 ratios (1.37 and 1.30 for AR-C239 an atropine resp.) obsd. in the control muscles at 6 h. The in vitro slowing is thus due to some change in the longitudinal muscle and not to a change in the receptors. The in vitro slowing occurred when either phenylephrine or methoxamine was the .alpha.1-adrenoceptor agonist used. The most likely mechanism of desensitization is a non-specific slowing of the access of drugs to receptors.  
 IT RL: BIOL (Biological study)  
 (vas deferens and anococcygeus muscle desensitization to)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-isoquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

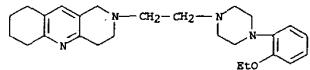


L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1984:103395 CAPLUS  
 DOCUMENT NUMBER: 100:103395  
 TITLE: 1,2,3,4,6,7,8,9-Octahydro-benzo[b]-1,6-naphthyridine derivatives  
 PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

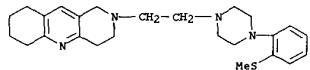
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58188884	A2	19831104	JP 1982-70338	19820428



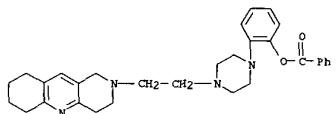
AB Title compds. I (R = MeS, ECO, BzO) were prep'd. by reaction of II (X = halo) with III (R = MeS, EtO) optically followed by hydrolysis and benzoylation. Antivertigo and muscle relaxant activity test data of I were shown in cats and mice, resp. Thus, refluxing a mixt. of II 2HCl (X = Cl) 4.9, III HCl (R = O-MeS) 3.7, and Et3N 7.6 g in EtOH 2 h gave 76% I (R = MeS), which was converted to the fumarate by treating with fumaric acid in MeCO.  
 IT 83081-77-0P 89009-91-6P 89009-92-7P  
 89009-94-9P 89009-98-0P 89009-96-1P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prep. and pharmacol. activities of)  
 RN 83081-77-0 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 89009-91-6 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylthio)phenyl]-1-piperazinyl]ethyl- (9CI) (CA INDEX NAME)



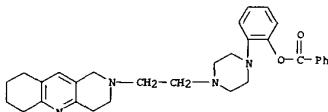
RN 89009-92-7 CAPLUS  
CN Phenol,  
2-[4-(2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl)-1-piperazinyl]-, benzoate (ester) (9CI) (CA INDEX NAME)



RN 89009-94-9 CAPLUS  
CN Phenol,  
2-[4-(2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl)-1-piperazinyl]-, benzoate (ester), (2E)-2-butenedioate (1:2) (salt) (9CI) (CA INDEX NAME)

CM 1

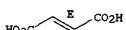
RN 89009-92-7  
CMF C31 H36 N4 O2



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

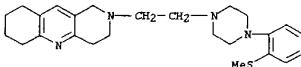
Double bond geometry as shown.



RN 89009-95-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylthio)phenyl]-1-piperazinyl]ethyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

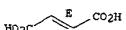
CRN 89009-91-6  
CMF C25 H34 N4 S



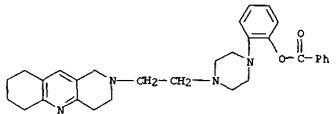
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 89009-96-1 CAPLUS  
CN Phenol,  
2-[4-(2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl)-1-piperazinyl]-, benzoate (ester), tetrahydrochloride (9CI) (CA INDEX NAME)



● HCl

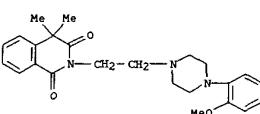
ACCESSION NUMBER: 1983-47179 CAPLUS  
DOCUMENT NUMBER: 99-97179  
TITLE: Structure of 2-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-1,3(2H,4H)-isoquinolinodione hydrochloride-ethanol (AR-C239), C24H30N3O3+.Cl-.C2H6O

AUTHOR(S): Carpy, Alain; Goursolle, Michel; Leger, Jean  
Michel  
CORPORATE SOURCE: Fac. Pharm., Univ. Bordeaux II, Bordeaux, 33076,  
Fr.  
SOURCE: Acta Crystallogr., Sect. C: Cryst. Struct.  
Commun.

DOCUMENT TYPE: (1983), C39(8), 1087-9  
CODEN: ACSCEE  
LANGUAGE: Journal  
French  
AB The title compd. is triclinic, space group P.hivin.1, was a 9.749(2), b 11.287(5), c 13.815(1) .ANG., .alpha. 77.43(2), .beta. 83.99(1), and .gamma. 69.96(3).degree.; Z = 2 for dc = 1.17. Final R = 0.070 for 2643 reflections. The bridge chain is in the fully extended conformation and is perpendicular to the isoquinoline plane. N-H...Cl H-bonds contribute to the cryst. cohesion. At. coordinates are given.  
IT 86891-01-2  
RL PRP (Properties)  
(structure of)  
RN 86891-01-2 CAPLUS  
CN 1,3(2H,4H)-Isoquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride, compd. with ethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 86891-00-1  
CMF C24 H29 N3 O3 . Cl H

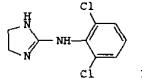


● HCl

CM 2  
CRN 64-17-5  
CMF C2 H6 O

H<sub>3</sub>C—CH<sub>2</sub>—OH

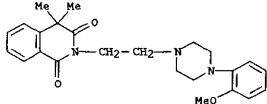
L14 ANSWER 222 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1983:432919 CAPLUS  
DOCUMENT NUMBER: 99:32919  
TITLE: Bronchopulmonary effects of clonidine on the  
Author(s): Advenier, Charles; Floch, Anne; Mallard, Brigitte  
CORPORATE SOURCE: Lab. Pharmacol., Fac. Med. Paris, Paris, F-75270,  
Fr.  
SOURCE: Eur. J. Pharmacol. (1983), 89(1-2), 85-94  
CODEN: EJPHAZ; ISSN: 0014-2999  
Journal English  
Language: Gt



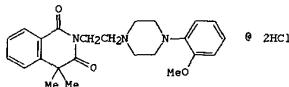
AB In conscious guinea pigs, clonidine (I) [4205-90-7] (10 and 100 .mu.g/kg, i.v.) lowered diastolic (-7.9 and -12.4%) and systolic (-8.6 and -11.9%) arterial pressure and reduced heart rate (-14.5 and -27.7%), but did not significantly modify pulmonary airway resistance. Hypotension was suppressed by yohimbine [146-48-5] and bradycardia was partially suppressed by atropine [51-55-8] and yohimbine, which demonstrates in this animal an .alpha.-2-adrenergic effect for hypotension and a mixed cholinergic and .alpha.-2-adrenergic effect for bradycardia. Clonidine (10 and 100 .mu.g/kg, i.v.) enhanced the bronchoconstrictor effects of histamine [51-45-6] 20 .mu.g/kg (+80.0 and 89.1%), acetylcholine [51-84-3] 25 .mu.g/kg (+66.4 and +95.4%) and serotonin creatinine sulfate [971-74-4] 15 .mu.g/kg (+68.5 and +81.4%). The duration of this effect was comparable to that of the hypotensive and cardiac effects of clonidine. The effects of clonidines were suppressed after pretreatment with propranolol [525-66-6], reserpine [50-55-5], or pentobarbital [76-74-4], all drugs which enhance the bronchoconstrictor effect of acetylcholine. Yohimbine (1 mg/kg), piperexan [59-39-2] (0.3 mg/kg) or prazosin [19216-56-9] in high dosage (0.3 mg/kg) inhibited the potentiation by clonidine of acetylcholine-induced bronchoconstriction, whereas prazosin in lower doses (0.03 mg/kg) or AR-C 239 [67339-62-2] (0.05 mg/kg) had no action. A specific involvement of .alpha.-2-adrenoceptors stimulated by clonidine with subsequent redn. of the adrenergic activity assoc'd. with bronchospasm could therefore be

IT 67339-62-2

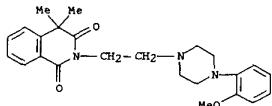
RL: BIO (Biological study)  
(bronchopulmonary effects of clonidine in relation to)  
RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 223 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1983:172852 CAPLUS  
DOCUMENT NUMBER: 98:172852  
TITLE: AR-C239 a new and potent .alpha.-adrenoceptor blocking drug  
Author(s): Mouille, P.; Huchet, A. M.; Chelly, J.; Schmitt, H.  
CORPORATE SOURCE: Lab. Pharmacol., Fac. Broussais, Paris, Fr.  
SOURCE: Alpha-Bloquants, Symp. Int. (1981), Meeting Date 1979,  
14-20. Masson: Paris, Fr.  
CODEN: 49LNA7  
Conference  
Language: English  
GI



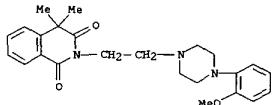
AB The pharmacol. effects of AR-C 239 (I) [67339-62-2] (30-50 mg/kg, i.v.) were investigated in anesthetized dogs. I produced a long-lasting fall in blood pressure and cardiac parameters, partly by acting peripherally and partly by central redn. of sympathetic nerve activity. I was specific for .alpha.1-postsynaptic adrenoceptors in dogs. The cardiovascular effects of clonidine and the baroreceptor reflex were unaffected by I, indicating that adrenoceptors implicated in these effects are of the .alpha.-2-type. I may be useful in the characterization of .alpha.-adrenoceptors.  
IT 67339-62-2  
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic); BIO (Biological study); USES (Uses)  
(pharmacol. of)  
RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 224 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1983:84010 CAPLUS  
 DOCUMENT NUMBER: 98:84010  
 TITLE: The .alpha.2-adrenergic receptor of human fat  
 cells: comparative study of .alpha.2-adrenergic  
 radioligand binding and biological response  
 AUTHOR(S): Berlan, Michel; Lafontan, Max  
 CORPORATE SOURCE: Fac. Med., Univ. Paul Sabatier, Toulouse,  
 F-31400, Fr.  
 SOURCE: J. Physiol. (Paris) (1982), 76(3), 279-87  
 CODEN: JOPHAN; ISSN: 0021-7948

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The binding of 3H-labeled yohimbine (I) [146-48-5], an .alpha.2-adrenergic antagonist, and clonidine (II) [4205-90-7], an .alpha.2-adrenergic agonist, on the human fat cell membrane .alpha.-adrenoceptor was compared. The relative order of affinity of various agonists and antagonists towards the .alpha.-receptor with their relative biol. potency when estd. by measuring the lipolysis rate of adipocytes in vitro were also compared. The specific binding of these 2 radioactive ligands was a saturable process. The estd. equil. dissocn. consts. (KD) were similar (4 nM for [3H]II, and 4.3 nM for [3H]I). The no. of [3H]I-binding sites per mg protein was apprx. 2-3 times higher than the no. of [3H]II-binding sites (350 fmol/mg protein). The relative order of potency of various .alpha.-agonists and .alpha.-antagonists in competition with the 2 radioligands was similar and was consistent with the delineation of an .alpha.2-adrenoceptor. For integrated anal. at the cellular level, the effect of the various .alpha.-adrenomimetics on theophylline and isoproterenol-induced lipolysis was also studied. Substances which possess .alpha.2-adrenomimetic potency induce an antilipolytic effect whereas .alpha.1-adrenomimetic drugs were without effect. Moreover the order of potency of .alpha.-antagonists in the suppression of the antilipolysis promoted by II is in good agreement with the involvement of an .alpha.2-adrenoceptor stimulation in the genesis of the inhibiting effect on lipolysis. The binding sites of I and II on human fat cell membranes apparently correspond to the physiol. .alpha.2-adrenergic receptors involved in the antilipolytic effect of catecholamines in human adipose tissue.

IT 67339-62-2  
 RL: PROC (Process)  
 (adrenergic receptor binding of, in adipocyte of human, lipolysis  
 in relation to)  
 RN 67339-62-2 CAPLUS  
 CN 1,3-(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-

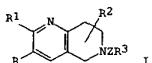


L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1983:72076 CAPLUS  
 DOCUMENT NUMBER: 98:72076  
 TITLE: 5,6,7,8-Tetrahydro-1,6-naphthyridine derivatives  
 INVENTOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Ishikawa, Michio; Miyazaki, Hiroshi; Yamanaka, Hiroshi  
 PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan  
 SOURCE: Fr. Demande, 108 pp.  
 CODEN: FRXXBL  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2492825	A1	19820430	FR 1981-20262	19811028
JP 57075983	A2	19820512	JP 1980-150719	19801029
ES 507200	A1	19830201	ES 1981-507200	19811029

PRIORITY APPLN. INFO.: JP 1980-150719 19801029

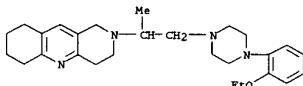
GI



AB Naphthyridines I (R and R1 are H, alkyl, or RR1 = C2-5 alkylene; R2 = H, alkyl, PhCH2, Ph, halo-, alkyl-, or alkoxyphenyl; Z = C2-4 alkylene; R3 = dialkylamino, 1-pyrrolidinyl, 1-piperidinyl, a 4-hydroxy-4-phenyl-1-piperidinyl group, 4-morpholinyl, a 4-substituted 1-piperazinyl group) were prep'd., and they showed anti-vertigo and muscle relaxant activity.  
 5,6,7,8-Tetrahydro-3-methyl-1,6-naphthyridine was treated with 1-(2-chloroethyl)-4-(2-chlorophenyl)piperazine-2HCl and Me3N to give I [R = Me, Z = CH2CH2, R3 = 4-(2-chlorophenyl)-1-piperazinyl, R1 = R2 = H].  
 IT 63081-72-5P  
 RL: SPC (Synthetic preparation); PREP (Preparation)  
 (prep. and anti-vertigo activity of)  
 RN 63081-72-5 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methyl-ethyl]-1,2,3,4,5,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2)  
 (SCI) (CA INDEX NAME)

CM 1

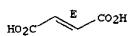
CRN 63081-71-4  
 CMF C27 H38 N4 O



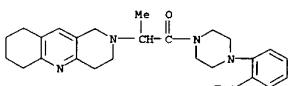
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

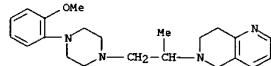


IT 83099-95-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prep. and hydride redn. of)  
RN 83099-95-0 CAPLUS  
CN Piperazine, 1-(2-methoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b](1,6)naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)



IT 83082-18-2P 83082-28-4P 84328-17-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. and muscle relaxant activity of)  
RN 83082-18-2 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)  
CM 1  
CRN 83082-17-1  
CMF C20 H25 F N4

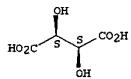
CM 1

CRN 83081-73-6  
CMF C22 H30 N4 O

CM 2

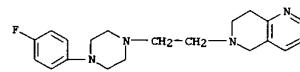
CRN 133-37-9  
CMF C4 H6 O6

Relative stereochemistry.



IT 83081-78-1P 83082-67-1P 83100-04-3P  
83100-14-5P 83100-18-9P 83100-36-1P  
83100-40-7P 84345-54-0P  
RL: BA (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prep. and pharmacol. activity of)  
RN 83081-78-1 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-  
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

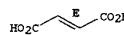
CM 1

CRN 83081-77-0  
CMF C26 H36 N4 O

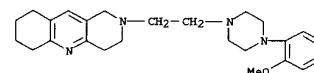
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



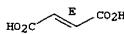
RN 83082-28-4 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)  
(CA INDEX NAME)  
CM 1  
CRN 83082-27-3  
CMF C25 H34 N4 O



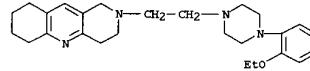
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



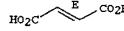
RN 84328-17-6 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2)



CM 2

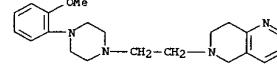
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 83082-67-1 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

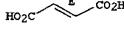
CM 1

CRN 83082-65-9  
CMF C21 H28 N4 O

CM 2

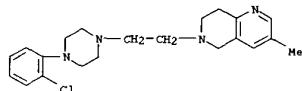
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 83100-04-3 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1  
CRN 83100-01-0  
CMF C21 H27 Cl N4

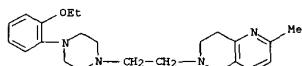


CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

CC(=O)C=C[C@H](C)C(=O)O  
RN 83100-14-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX  
NAME)

CH 1  
CRN 83100-13-4  
CMF C23 H32 N4 O



CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

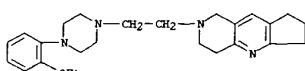
Double bond geometry as shown.

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

CC(=O)C=C[C@H](C)C(=O)O  
RN 83100-40-7 CAPLUS  
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-(4-(2-ethoxyphenyl)-1-  
piperazinyl)ethyl]-2,3,4,6,7,8-hexahydro-, (2E)-2-butenedioate (1:2)  
(9CI) (CA INDEX NAME)

CH 1  
CRN 83100-39-4  
CMF C25 H34 N4 O



CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

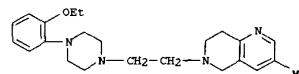
Double bond geometry as shown.

CC(=O)C=C[C@H](C)C(=O)O  
RN 84345-54-0 CAPLUS  
CN 1,6-Naphthyridine,  
5,6,7,8-tetrahydro-2-methyl-6-[2-(4-(2-methylphenyl)-1-  
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CH 1  
CRN 83100-11-2  
CMF C22 H30 N4

CC(=O)C=C[C@H](C)C(=O)O  
RN 83100-18-9 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1  
CRN 83100-17-8  
CMF C23 H32 N4 O

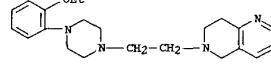


CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

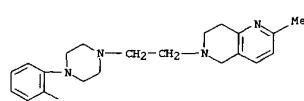
Double bond geometry as shown.

CC(=O)C=C[C@H](C)C(=O)O  
RN 83100-36-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-  
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1  
CRN 83100-35-0  
CMF C22 H30 N4 O



CH 2

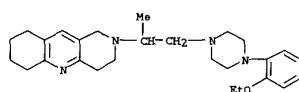


CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

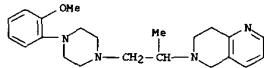
Double bond geometry as shown.

CC(=O)C=C[C@H](C)C(=O)O  
IT 83081-71-4P 83081-73-6P 83081-74-7P  
83081-77-0P 83082-17-1P 83082-23-9P  
83082-24-0P 83082-27-3P 83082-29-5P  
83082-30-8P 83082-37-5P 83082-59-1P  
83082-60-4P 83082-61-5P 83082-62-6P  
83082-63-7P 83082-64-8P 83082-65-9P  
83082-66-0P 83082-67-1P 83100-13-4P  
83100-17-9P 83100-19-5P 83100-20-4P  
83100-21-4P 83100-22-5P 83100-23-6P  
83100-24-7P 83100-25-6P 83100-26-5P  
83100-27-0P 83100-35-0P 83100-37-2P  
83100-38-3P 83100-39-4P 84414-63-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 83081-71-4 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)-1-  
methyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

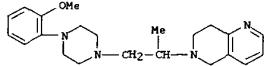


RN 83081-73-6 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-(2-(4-(2-methoxyphenyl)-1-  
piperazinyl)-1-methyl)- (9CI) (CA INDEX NAME)



RN 83081-74-7 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-(2-(4-(2-methoxyphenyl)-1-piperazinyl)-1-methylethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

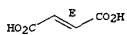
CH 1

CRN 83081-73-6  
CMF C22 H30 N4 O

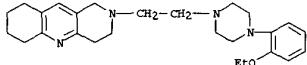
CH 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

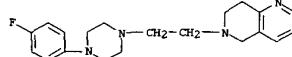
Double bond geometry as shown.



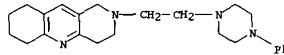
RN 83081-77-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-(2-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-  
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83082-17-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-(2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl)-5,6,7,8-

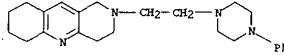


RN 83082-23-9 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
1,2,3,4,6,7,8,9-octahydro-2-(2-(4-phenyl-1-piperazinyl)ethyl)- (9CI) (CA INDEX NAME)



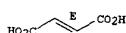
RN 83082-24-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
1,2,3,4,6,7,8,9-octahydro-2-(2-(4-phenyl-1-piperazinyl)ethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

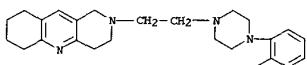
CRN 83082-23-9  
CMF C24 H32 N4

CH 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

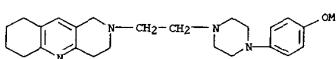
Double bond geometry as shown.



RN 83082-27-3 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

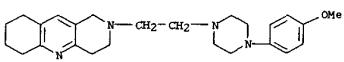


RN 83082-29-5 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

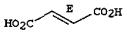
CH 1

CRN 83082-29-5  
CMF C25 H34 N4 O

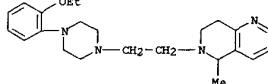
CH 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

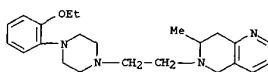
Double bond geometry as shown.



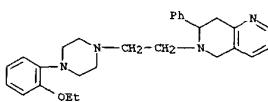
RN 83082-37-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-5-methyl- (9CI) (CA INDEX NAME)



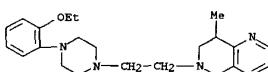
RN 83082-59-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-(2-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 83082-60-4 CAPLUS  
CN 1,6-Naphthyridine,  
6-(2-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-7-phenyl- (9CI) (CA INDEX NAME)

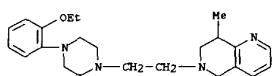


RN 83082-61-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-methyl- (9CI) (CA INDEX NAME)



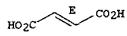
RN 83082-62-6 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1  
CRN 83082-61-5  
CMF C23 H32 N4 O

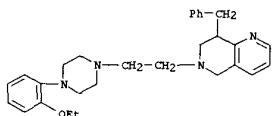


CM 2  
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

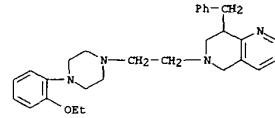


RN 83082-63-7 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-(phenylmethyl)-(9CI) (CA INDEX NAME)



RN 83082-64-8 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-(phenylmethyl)-(2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

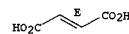
CM 1  
CRN 83082-63-7  
CMF C29 H36 N4 O



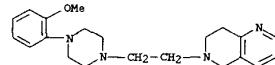
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

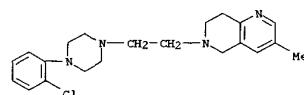
Double bond geometry as shown.



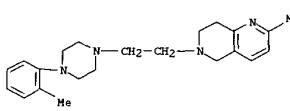
RN 83082-65-9 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-(9CI) (CA INDEX NAME)



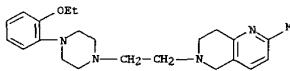
RN 83100-01-0 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-3-methyl-(9CI) (CA INDEX NAME)



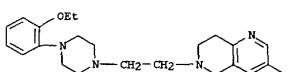
RN 83100-11-2 CAPLUS  
CN 1,6-Naphthyridine,  
5,6,7,8-tetrahydro-2-methyl-6-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-(9CI) (CA INDEX NAME)



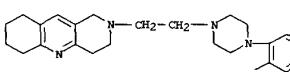
RN 83100-13-4 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-2-methyl-(9CI) (CA INDEX NAME)



RN 83100-17-8 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-3-methyl-(9CI) (CA INDEX NAME)

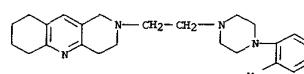


RN 83100-19-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-(9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-(2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

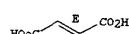
CM 1  
CRN 83100-19-0  
CMF C25 H34 N4



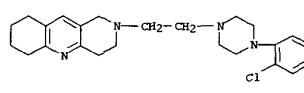
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

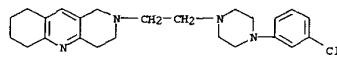
Double bond geometry as shown.



RN 83100-21-4 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]-1,2,3,4,6,7,8,9-octahydro-(9CI) (CA INDEX NAME)



RN 83100-22-5 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-1,2,3,4,6,7,8,9-octahydro-(9CI) (CA INDEX NAME)

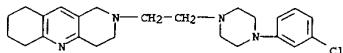


RN 83100-23-6 CAPLUS

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-{4-(3-chlorophenyl)-1-piperazinyl}ethyl]-  
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

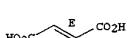
CRN 83100-22-5  
 CMF C24 H31 Cl N4



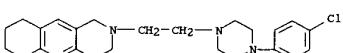
CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



RN 83100-24-7 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-{4-(4-chlorophenyl)-1-piperazinyl}ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

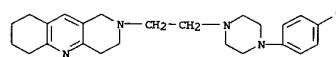


RN 83100-25-8 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-{4-(4-chlorophenyl)-1-piperazinyl}ethyl]-  
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-24-7  
 CMF C24 H31 Cl N4

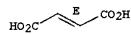
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



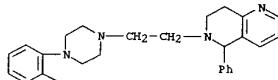
CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



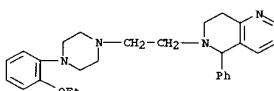
RN 83100-26-9 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-5,6,7,8-tetrahydro-5-phenyl- (9CI) (CA INDEX NAME)



RN 83100-27-0 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-5,6,7,8-tetrahydro-5-phenyl-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-26-9  
 CMF C28 H34 N4 O

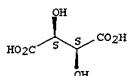


L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

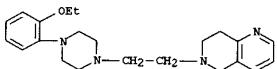
CM 2

CRN 133-37-9  
 CMF C4 H6 O6

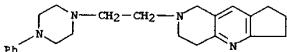
Relative stereochemistry.



RN 83100-35-0 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 83100-37-2 CAPLUS  
 CN 1H-Cyclopenta[b][1,6]naphthyridine,  
 2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

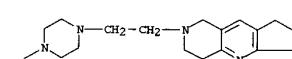


RN 83100-38-3 CAPLUS  
 CN 1H-Cyclopenta[b][1,6]naphthyridine,  
 2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-37-2  
 CMF C23 H30 N4

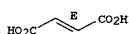
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



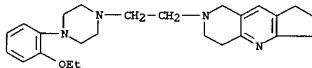
CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



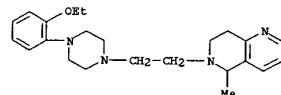
RN 83100-39-4 CAPLUS  
 CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-2,3,4,6,7,8-hexahydro- (9CI) (CA INDEX NAME)



RN 84414-63-1 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-{4-(2-ethoxyphenyl)-1-piperazinyl}ethyl]-5,6,7,8-tetrahydro-5-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

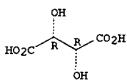
CRN 93092-37-5  
 CMF C23 H32 N4 O



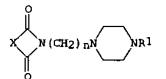
CM 2

CRN 87-69-4  
CME C4 H6 O6  
CDES 1:R2:R\*,R\*

Absolute stereochemistry.

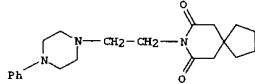


L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1983:46453 CAPLUS  
DOCUMENT NUMBER: 98:46453  
TITLE: Buspirone analogs. I. Structure-activity relationships in a series of N-aryl- and heteroarylpirazine derivatives  
AUTHOR(S): Yevich, J. P.; Temple, D. L., Jr.; New, J. S.; Taylor, L. A.  
CORPORATE SOURCE: CNS Res.-Pharm. Res. Dev. Div., Bristol-Myers Co., Evansville, IN, 47721, USA  
SOURCE: J. Med. Chem. (1983), 26(2), 194-203  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 98:46453  
GI

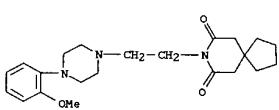


I

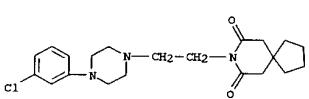
AB The title compds. I (X = substituted cyclic imide; R1 = substituted Ph, substituted pyridyl or substituted pyrimidinyl; n = 2-4) as the HCl salts were prepd. by the reaction of the appropriate piperazinebutanamine with the corresponding cyclic oxy compd. or by the reaction of a substituted piperazine with the corresponding cyclic imide. I and related analogs were tested *in vitro* for the binding affinities to rat brain membrane sites labeled with either the dopamine antagonist [<sup>3</sup>H]spiperone or the  $\alpha$ .<sub>1</sub>-adrenergic antagonist [<sup>3</sup>H]WB-4101 and *in vivo* for tranquilizing properties and induction of catalepsy. The azaspirodecanedione moiety affords the strongest affinity for dopaminergic binding sites and the most selectivity relative to  $\alpha$ .<sub>1</sub>-adrenergic blocking potential. Structure-activity relations are discussed.  
IT 21090-07-3 21102-54-3 21102-20-8  
25024-93-5 25024-94-6 83928-69-2  
63928-77-2 83928-78-3  
RL: BIOL (Biological study)  
RN 21090-07-3 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



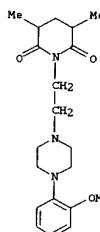
RN 21102-94-3 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-{4-(2-methoxyphenyl)-1-piperazinyl}ethyl]- (9CI) (CA INDEX NAME)



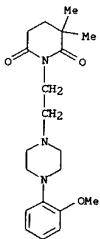
RN 21103-20-8 CAPLUS  
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-{4-(3-chlorophenyl)-1-piperazinyl}ethyl]- (9CI) (CA INDEX NAME)



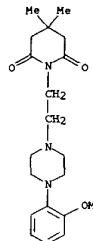
RN 25024-93-5 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-{4-(2-methoxyphenyl)-1-piperazinyl}ethyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)



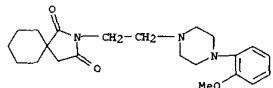
RN 25024-94-6 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-{4-(2-methoxyphenyl)-1-piperazinyl}ethyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)



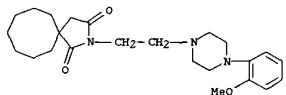
RN 83928-69-2 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-{4-(2-methoxyphenyl)-1-piperazinyl}ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



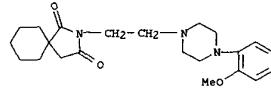
RN 83928-77-2 CAPLUS  
CN 2-Azaspido[4.5]deca-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83928-78-3 CAPLUS  
CN 2-Azaspido[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

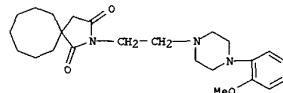


IT 83928-67-0 83928-68-1  
RL: BIOL (Biological study)  
(pre-treatment and anxiolytic and receptor binding activities of)  
RN 83928-67-0 CAPLUS  
CN 2-Azaspido[4.5]deca-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



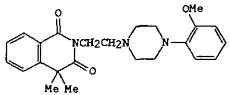
● 2 HCl

RN 83928-68-1 CAPLUS  
CN 2-Azaspido[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 227 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1983:27864 CAPLUS  
DOCUMENT NUMBER: 98:27864  
TITLE: Possible role of central .alpha.1-adrenoceptors  
in the control of the autonomic nervous system in normotensive and spontaneously hypertensive rats  
AUTHOR(S): Huchet, Anne Marie; Douroux, Marie Francoise;  
Chelli, Jacques; Schmitt, Henri  
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med. Broussais-Hotel Dieu,  
Paris, 75006, Fr.  
SOURCE: Eur. J. Pharmacol. (1982), 85(2), 239-42  
CODEN: EJPMAZ; ISSN: 0014-2999  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI

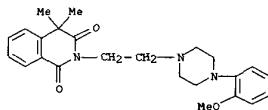


AB The cardiovascular effects of AR-C 239 (I) [67339-62-2], a new and selective .alpha.1-adrenoceptor blocking drug, were studied in normotensive and spontaneously hypertensive rats (SHR). AR-C 239 (300 .mu.g/kg, i.v.) did not change the heart rate in control (without pretreatment) and bilaterally vagotomized normotensive rats, but induced significant bradycardia in rats pretreated with a .beta.-adrenoceptor blocking drug. The bradycardic effect was inhibited by atropine or bilateral vagotomy. In SHR, the administration of AR-C 239 reduced heart rate in the control, bilaterally vagotomized and .beta.-blocked rats. Blood pressure was decreased in the same way in the 2 rat strains.

Apparently, central .alpha.1-adrenoceptors could participate in the control of vagal tone in normotensive and SH rats, and of sympathetic activity in the SHR only.

IT 67339-62-2  
RL: BIOL (Biological study)  
(nervous system response to, in hypertension, adrenoceptors in relation to)

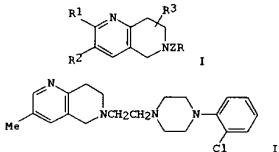
RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-Isquinolinodione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1982:54076 CAPLUS  
 DOCUMENT NUMBER: 97:144976  
 TITLE: 5,6,7,8-tetrahydro-1,6-naphthyridine derivatives  
 INVENTOR(S): Shiozawa, Akira; Iizakawa, Yuhichiro; Ishihara, Michiori; Miyazaki, Hiroshi  
 PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan  
 SOURCE: Ger. Offen., 109 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3143016	A1	19820527	DE 1981-3143016	19811029
JP 57075983	A2	19820512	JP 1980-150719	19801029
JP 58057379	A2	19830405	JP 1981-154863	19811001
SE 8106359	A	19820430	SE 1981-6359	19811028
GB 2087390	A	19820526	GB 1981-32554	19811029
GB 2087390	B2	19840613		
ES 516935	A1	19840216	ES 1982-516935	19821015
PRIORITY APPLN. INFO.:			JP 1980-150719	19801029
			JP 1981-154863	19811001

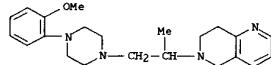
GI



AB The title naphthyridines I (R = dialkylamino, pyrrolidinyl, hydroxymethylpiperidinyl, 1-morpholinyl, 4-alkyl-, 4-benzyl-, 4-pyridyl-, or 4-(un)substituted-phenylpiperazinyl; R1, R2 = alkyl, R1R2 = C2-5 alkylene; R3 = H, alkyl, Bz, R4C6H4 (R4 = H, halo, alkyl, alkoxy); Z = C2-4 alkylene), useful in treatment of vertigo and as muscle relaxants (data tabulated), were prep'd. Alkylation of 5,6,7,8-tetrahydro-3-methyl-1,6-naphthyridine with 1-(2-chloromethyl)-4-(2-chlorophenyl)piperazine-2HCl in EtOH-NEt3 gave 41% naphthyridine II, which was converted to its difumarate.

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 IT 83081-74-7 CAPLUS  
 RL: RCT (Reactant)  
 (muscle relaxant activity of)  
 RN 83081-74-7 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

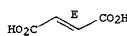
CM 1  
 CRN 83081-73-6  
 CMF C22 H30 N4 O



CM 2

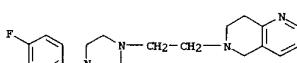
CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.



RN 83082-18-2 CAPLUS  
 CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

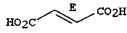
CM 1  
 CRN 83082-17-1  
 CMF C20 H25 F N4



CM 2

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

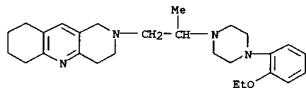
Double bond geometry as shown.



IT 83081-60-1  
 RL: RCT (Reactant)  
 (nystagmus inhibitory activity of)  
 RN 83081-60-1 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-  
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

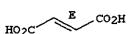
CRN 83081-59-8  
 CMF C27 H38 N4 O



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

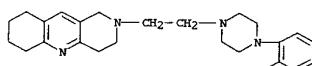
Double bond geometry as shown.



IT 83082-28-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. and muscle relaxant activity of)  
 RN 83082-28-4 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

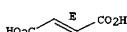
CM 1  
 CRN 83082-27-3  
 CMF C25 H34 N4 O



CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

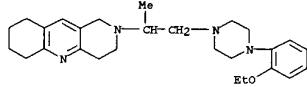
Double bond geometry as shown.



IT 83081-72-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. and nystagmus inhibitory activity of)  
 RN 83081-72-5 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

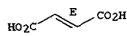
CRN 83081-71-4  
 CMF C27 H38 N4 O



CM 2

CRN 110-17-8  
 CMF C4 H4 O4

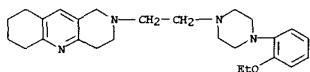
Double bond geometry as shown.



IT 83081-78-1P 83082-67-1P 83100-04-3P  
83100-12-3P 83100-14-5P 83100-18-9P  
83100-36-1P 83100-40-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep., and nystagmus inhibitory and muscle relaxant activity of)  
RN 83081-78-1 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-  
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

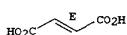
CRN 83081-77-0  
CMF C26 H36 N4 O



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 83082-67-1 CAPLUS  
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

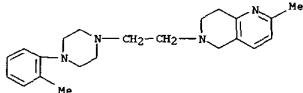
CM 1

CRN 83082-65-9  
CMF C21 H28 N4 O

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
Double bond geometry as shown.  
CDES 2:E

CM 1

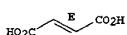
CRN 83100-11-2  
CMF C22 H30 N4



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

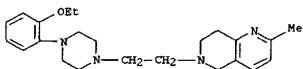
Double bond geometry as shown.



RN 83100-14-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

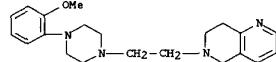
CM 1

CRN 83100-13-4  
CMF C23 H32 N4 O



CM 2

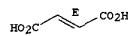
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

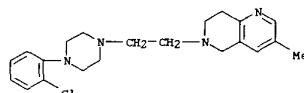
Double bond geometry as shown.



RN 83100-04-3 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

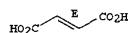
CRN 83100-01-0  
CMF C21 H27 Cl N4



CM 2

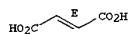
CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



RN 83100-12-3 CAPLUS  
CN 1,6-Naphthyridine,  
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-

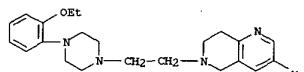
Double bond geometry as shown.



RN 83100-18-9 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

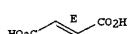
CRN 83100-17-8  
CMF C23 H32 N4 O



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

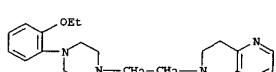
Double bond geometry as shown.



RN 83100-36-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

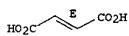
CRN 83100-35-0  
CMF C22 H30 N4 O



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

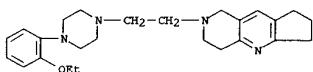
Double bond geometry as shown.



RN 83100-40-7 CAPLUS  
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

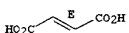
CRN 83100-39-4  
CMF C25 H34 N4 O



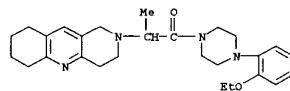
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

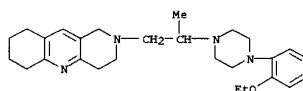


IT 83099-95-0  
RN: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and redn. of)  
83099-95-0 CAPLUS  
CN: Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl] - (9CI) (CA INDEX NAME)

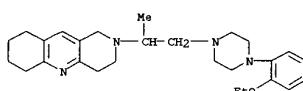


IT 83081-59-8P 83081-71-4P 83081-73-6P  
83081-74-7P 83081-76-9P 83081-77-0P  
83082-17-1P 83082-23-9P 83082-24-0P  
83082-27-3P 83082-29-5P 83082-30-8P  
83082-37-5P 83082-38-6P 83082-59-1P  
83082-60-4P 83082-61-5P 83082-62-6P  
83082-63-7P 83082-64-8P 83082-65-9P  
83100-17-8P 83100-19-1P 83100-20-2P  
83100-21-4P 83100-22-5P 83100-23-6P  
83100-24-7P 83100-25-8P 83100-26-9P  
83100-27-0P 83100-35-0P 83100-37-2P  
83100-38-3P 83100-39-4P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

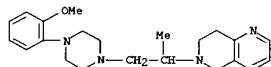
RN 83081-59-1 CAPLUS  
CN: Benzo[b][1,6]naphthyridine,  
2-[2-(2-ethoxyphenyl)-1-piperazinyl]propyl-  
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



IT 83081-71-4 CAPLUS  
CN: Benzo[b][1,6]naphthyridine, 2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



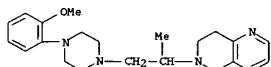
RN 83081-73-6 CAPLUS  
CN: 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-(2-methoxyphenyl)-1-



RN 83081-74-7 CAPLUS  
CN: 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (CA INDEX NAME)

CM 1

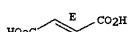
CRN 83081-73-6  
CMF C22 H30 N4 O



CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

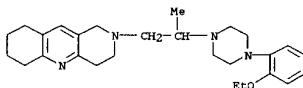
Double bond geometry as shown.



RN 83081-76-9 CAPLUS  
CN: Benzo[b][1,6]naphthyridine,  
2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)propyl]-  
1,2,3,4,6,7,8,9-octahydro-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

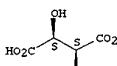
CRN 83081-59-8  
CMF C27 H38 N4 O



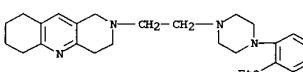
CM 2

CRN 133-37-9  
CMF C4 H6 O6

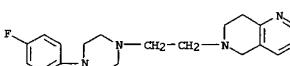
Relative stereochemistry.



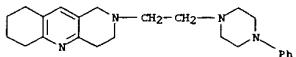
RN 83081-77-0 CAPLUS  
CN: Benzo[b][1,6]naphthyridine,  
2-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-  
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83082-17-1 CAPLUS  
CN: 1,6-Naphthyridines,  
6-[2-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

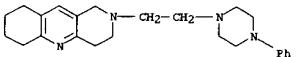


RN 83082-23-9 CAPLUS  
CN: Benzo[b][1,6]naphthyridine,  
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-24-0 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

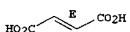
CM 1

CRN 83082-23-9  
CMF C24 H32 N4

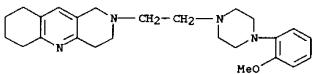
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



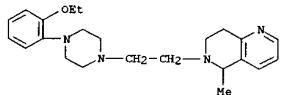
RN 83082-27-3 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-29-5 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

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tetrahydro-5-methyl-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI)  
(CA INDEX NAME)

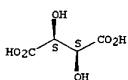
CM 1

CRN 83082-37-5  
CMF C23 H32 N4 O

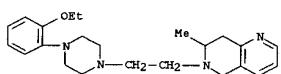
CM 2

CRN 133-37-9  
CMF C4 H6 O6

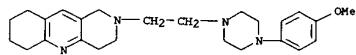
Relative stereochemistry.



RN 83082-59-1 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)

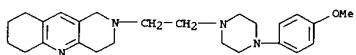


RN 83082-60-4 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-7-phenyl- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS  
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)  
(CA INDEX NAME)

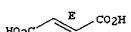
CM 1

CRN 83082-29-5  
CMF C25 H34 N4 O

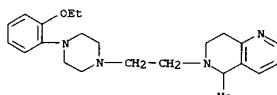
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

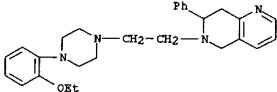


RN 83082-37-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-5-methyl- (9CI) (CA INDEX NAME)

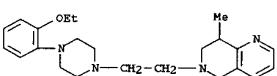


RN 83082-38-6 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-

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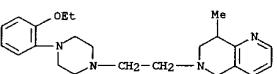


RN 83082-61-5 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 83082-62-6 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-(4-(2-ethoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

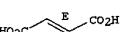
CM 1

CRN 83082-61-5  
CMF C23 H32 N4 O

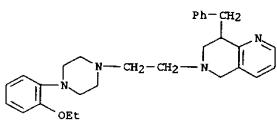
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.



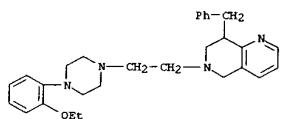
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 83082-63-7 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 83082-64-8 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-(phenylmethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

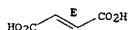
CRN 83082-63-7  
 CMF C29 H36 N4 O



CM 2

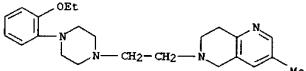
CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.

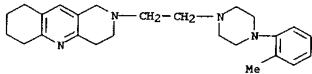


RN 83082-65-9 CAPLUS  
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



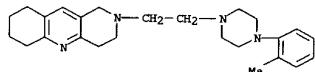
RN 83100-19-0 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS  
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

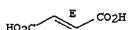
CRN 83100-19-0  
 CMF C25 H34 N4



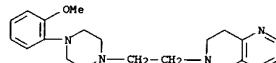
CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

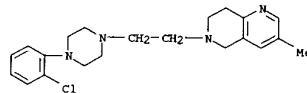
Double bond geometry as shown.



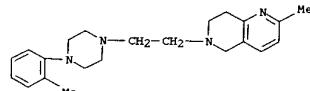
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 piperazinyl]ethyl)- (9CI) (CA INDEX NAME)



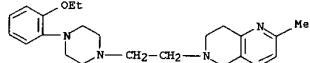
RN 83100-01-0 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



RN 83100-11-2 CAPLUS  
 CN 1,6-Naphthyridine,  
 5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



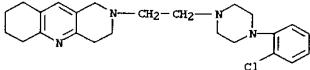
RN 83100-13-4 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



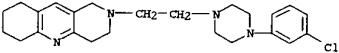
RN 83100-17-8 CAPLUS  
 CN 1,6-Naphthyridine,  
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 83100-21-4 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



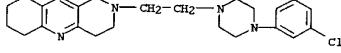
RN 83100-22-5 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-  
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-23-6 CAPLUS  
 CN Benzo[b][1,6]naphthyridine,  
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-  
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

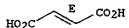
CRN 83100-22-5  
 CMF C24 H31 Cl N4



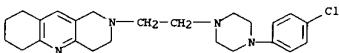
CM 2

CRN 110-17-8  
 CMF C4 H4 O4  
 CDES 2:E

Double bond geometry as shown.

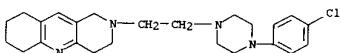


RN 83100-24-7 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-  
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-25-8 CAPLUS  
CN Benzo[b][1,6]naphthyridine,  
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-  
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-24-7  
CMF C24 H31 Cl N4 O

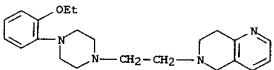
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

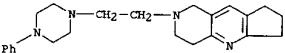
Double bond geometry as shown.



RN 83100-26-9 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-5-phenyl- (9CI) (CA INDEX NAME)

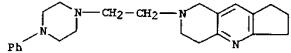


RN 83100-37-2 CAPLUS  
CN 1H-Cyclopenta[b][1,6]naphthyridine,  
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83100-39-3 CAPLUS  
CN 1H-Cyclopenta[b][1,6]naphthyridine,  
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

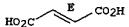
CM 1

CRN 83100-37-2  
CMF C23 H30 N4

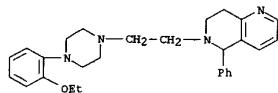
CM 2

CRN 110-17-8  
CMF C4 H4 O4  
CDES 2:E

Double bond geometry as shown.

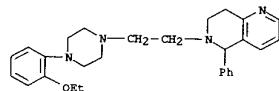


RN 83100-39-4 CAPLUS  
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro- (9CI) (CA INDEX NAME)



RN 83100-27-0 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-5-phenyl-, (R\*,R\*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

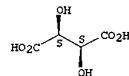
CM 1

CRN 83100-26-9  
CMF C28 H34 N4 O

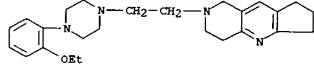
CM 2

CRN 133-37-9  
CMF C4 H6 O6

Relative stereochemistry.

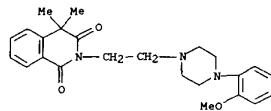


RN 83100-35-0 CAPLUS  
CN 1,6-Naphthyridine,  
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

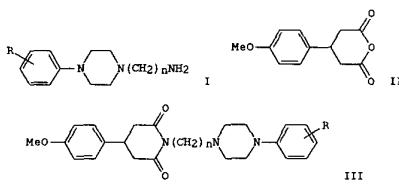


L14 ANSWER 229 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1982:538576 CAPLUS  
 DOCUMENT NUMBER: 97:138576  
 TITLE: GTP regulates binding of agonists to  
 .alpha.2-adrenergic receptors in human platelets  
 AUTHOR(S): Brodde, O. E.; Hardung, A.; Ebel, H.; Bock, K. D.  
 CORPORATE SOURCE: Med. Klin. Poliklin., Univ. Essen, Essen,  
 D-4300, Fed.  
 SOURCE: Rep. Ger.  
 193-207 Arch. Int. Pharmacodyn. Ther. (1982), 258(2),  
 DOCUMENT TYPE: CODEN: AIPTAZ; ISSN: 0003-9780  
 LANGUAGE: English  
 AB The potent .alpha.2-adrenergic receptor antagonist 3H-labeled  
 yohimbine [146-48-5] was used to characterize .alpha.-adrenergic receptors in  
 human platelet membranes. Binding of [3H]yohimbine at 25. degree. was  
 rapid (t1/2 = 3 min), readily reversible (t1/2 = 5.5 min), saturable with  
 221 fmoles bound/mg protein, and of high affinity (KD = 1.97 nM).  
 Inhibition of binding by .alpha.-adrenergic antagonists showed monophasic  
 displacement curves with Hill-coeffs. of approx. 1.0. The rank  
 order of potency was: rauwolscine [131-03-3] > yohimbine >  
 phenolamine [50-60-2] > phenoxybenzamine [59-96-1] > AR-C 239 [67339-62-2]  
 indicating that the .alpha.-adrenergic receptor in human platelets is of the  
 .alpha.2-subtype. On the contrary, agonist (clonidine) [4205-90-7],  
 guanfacine [29110-47-2], (-)-alpha.-methylnoradrenaline  
 [1829-74-3], (-)-noradrenaline [51-41-2] and (-)-adrenaline [51-43-4]  
 displacement curves were shallow with Hill-coeffs. of approx. 0.7. Non-linear  
 regression anal. showed that agonists bind to 2 affinity states of  
 the .alpha.2-adrenergic receptor, a high and a low affinity state. In  
 the presence of GTP [86-01-1] (10-14 M) agonist concn.-inhibition  
 curves were shifted to the right to lower affinities and Hill-coeffs. increased  
 up to 1.0. KI values for inhibition of binding in the presence of GTP  
 were in the same range as those for low affinity state in the absence of GTP.  
 Apparently, GTP regulates binding of .alpha.2-adrenergic agonists at  
 the human .alpha.2-adrenergic receptor.  
 IT 67339-62-2  
 RL: PROC (Process)  
 (binding of, to .alpha.-adrenergic receptors of blood platelets of  
 humans)

L14 ANSWER 229 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-  
 piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

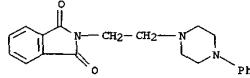


L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1981:550591 CAPLUS  
 DOCUMENT NUMBER: 95:150591  
 TITLE: Synthesis and pharmacology of 1-(4-aryl-1-  
 piperazinylalkyl)-4-(4-methoxyphenyl)piperidine-2,6-  
 diones: tranquilizers  
 AUTHOR(S): Samant, S. D.; Kulakarni, R. A.  
 CORPORATE SOURCE: Dep. Chem., Ramnarain Ruia Coll., Bombay, 400  
 019,  
 SOURCE: India J. Indian Chem. Soc. (1981), 58(7), 692-4  
 DOCUMENT TYPE: CODEN: JICSAH; ISSN: 0019-4522  
 LANGUAGE: Journal English  
 GI

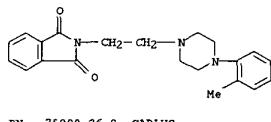


AB Condensation of piperazines I (R = H, 2-, 3-, 4-Me, 2-, 3-, 4-Cl; n = 2, 3) with II gave 24-63% the title compds. (III). III (R = H, n = 2) has an amphetamine antagonist ED50 of 38 mg/kg s.c. in mice.  
 IT 75000-24-7 75000-25-8 75000-26-9  
 75000-27-0 75000-28-1 75000-29-2  
 75000-30-5  
 RL: RCT (Reactant)  
 (hydrolysis of)  
 RN 75000-24-7 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

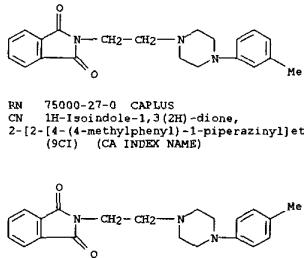
L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



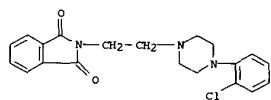
RN 75000-25-8 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



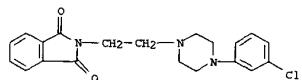
RN 75000-26-9 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



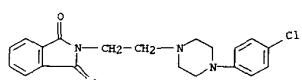
RN 75000-28-1 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



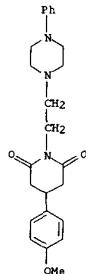
RN 75000-29-2 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione,  
 2-(2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl)-  
 (9CI) (CA INDEX NAME)



RN 75000-30-5 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione,  
 2-(2-(4-(4-chlorophenyl)-1-piperazinyl)ethyl)-  
 (9CI) (CA INDEX NAME)

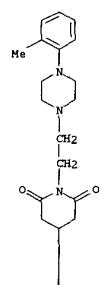


IT 79322-94-6P 79322-95-5P 79322-96-6P  
 79322-97-7P 79322-98-8P 79322-99-9P  
 79322-99-5P  
 RL: SRN (Synthetic preparation); PREP (Preparation)  
 (prepn. and central nervous system depressant activity of)  
 RN 79322-94-4 CAPLUS  
 CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-phenyl)-1-  
 piperazinyl]ethyl- (9CI) (CA INDEX NAME)



RN 79322-95-5 CAPLUS  
 CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-(2-methylphenyl)-1-  
 piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

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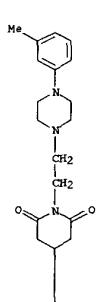
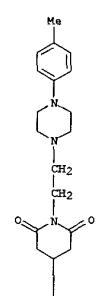


RN 79322-96-6 CAPLUS  
 CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-(3-methylphenyl)-1-  
 piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

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RN 79322-97-7 CAPLUS  
 CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-(4-methylphenyl)-1-  
 piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

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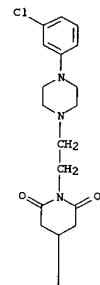
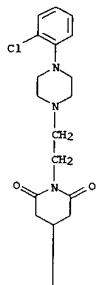


PAGE 2-A

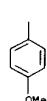
RN 79322-98-8 CAPLUS  
 CN 2,6-Piperidinedione,  
 1-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]-4-(4-  
 methoxyphenyl)- (9CI) (CA INDEX NAME)

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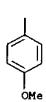
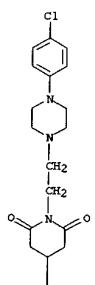


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RN 79322-99-9 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

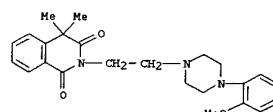
RN 79323-00-5 CAPLUS  
CN 2,6-Piperidinedione,  
1-[2-(4-(4-chlorophenyl)-1-piperazinyl)ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

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L14 ANSWER 231 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1981:490956 CAPLUS  
DOCUMENT NUMBER: 95:90956  
TITLE: Role of .alpha.1- and .alpha.2-adrenoceptors in  
the modulation of the baroreflex vagal bradycardia  
AUTHOR(S): Huchet, Anne Marie; Chelly, Jacques; Schmitt,  
Henri  
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med., Paris, 75270/06, Fr.  
SOURCE: Eur. J. Pharmacol. (1981), 71(4), 455-61  
CODEN: EJPHAZ; ISSN: 0014-2999  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Yohimbine-HCl [65-19-0] (100 .mu.g/kg), an .alpha.2-adrenoceptor  
blocking agent when injected into the vertebral artery of anesthetized dogs  
decreased the vagally mediated bradycardia induced by carotid sinus  
nerve stimulation. Intracisternal administration of phenylephrine-HCl  
(61-76-7) (30 .mu.g/kg) an .alpha.1-adrenoceptor agonist decreased,  
whereas AR-C 239-HCl [78448-19-8] (5 .mu.g/kg) and prazosin-HCl  
(19237-84-4) (5 .mu.g/kg) 2 potent .alpha.1-adrenoceptor antagonists  
injected into the vertebral artery, potentiated the bradycardic  
response.  
These results suggest, the presence of 2 types of  
.alpha.-adrenoceptors to  
modulate the baroreceptor pathway: .alpha.1-adrenoceptors inhibit and  
.alpha.2-adrenoceptors facilitates the transmission of baroreceptor  
impulses.  
IT 78448-19-8  
RL: BIOL (Biological study)  
(bradycardia response to, baroreflex in relation to)  
RN 78448-19-8 CAPLUS  
CN 1,3(2H,4H)-1aquinolinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



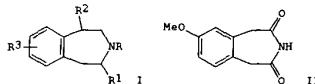
●x HCl

L14 ANSWER 232 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1981:47157 CAPLUS  
 DOCUMENT NUMBER: 94:47157  
 TITLE: Substituted 1,2,4,5-tetrahydro-3H,3 benzazepines  
 INVENTOR(S): Shetty, Bala V.  
 PATENT ASSIGNEE(S): Pennwalt Corp., USA  
 SOURCE: U.S., 30 pp. Division of U.S. Ser. No. 747,151,  
 abandoned.  
 CODEN: USXXAM

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

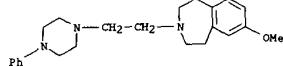
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4210749	A	19800701	US 1979-41574	19790521
US 4233217	A	19801111	US 1979-41575	19790521
PRIORITY APPLN. INFO.:			US 1968-711897	19680311
			US 1972-241091	19720404
			US 1974-523092	19741112
			US 1976-747151	19761203

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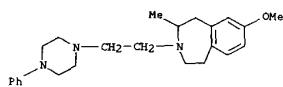


AB Benzazepines I ( $R = H$ , alkyl, alkenyl, aralkenyl, cycloalkylalkyl, aralkyl, heterocyclic alkyl;  $R_1 = H$ , alkyl, Ph, phenylalkyl;  $R_2 = H$ , alkyl;  $R_3 = H$ , alkoxy, alkyl, halo, NO<sub>2</sub>, HO), useful as analgesics and narcotic antagonists, were prep'd. Thus, treatment of 3,4-(NCCH<sub>2</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>Ome with HBr-AcO followed by heating at 85.degree. with NaOAc gave II, which was treated with BH<sub>3</sub> to give I ( $R = R_1 = R_2 = H$ ;  $R_3 = MeO$ ) (II). Refluxing III in 48% HBr gave I ( $R = R_1 = R_2 = H$ ;  $R_3 = HO$ ).  
 IT 36134-35-7P 76216-21-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepa. and pharmacol. of)  
 RN 36134-35-7 CAPLUS  
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 232 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

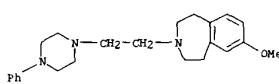


RN 76216-21-2 CAPLUS  
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-8-methoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



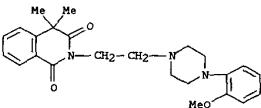
● 2 HCl

IT 36134-36-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)  
 RN 36134-36-8 CAPLUS  
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

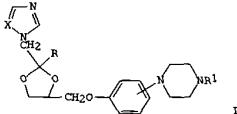
L14 ANSWER 233 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1981:44562 CAPLUS  
 DOCUMENT NUMBER: 94:44562  
 TITLE: Identification of .alpha.2-adrenergic receptors in human fat cell membranes by [<sup>3</sup>H]-clonidine binding  
 AUTHOR(S): Berlan, Michel; Lafontan, Max  
 CORPORATE SOURCE: Lab. Physiol. Appl. Pharmacol. Med., Fac. Med., Toulouse, F-31000, Fr.  
 SOURCE: Eur. J. Pharmacol. (1980), 67(4), 481-4  
 CODEN: EJPRAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB [<sup>3</sup>H]clonidine bound to membrane sites of human fat cells, which have the characteristics of .alpha.2-adrenoceptors. Specific binding was rapid, reversible, and saturable. [<sup>3</sup>H]clonidine binding was of high affinity with a KD of 3.9 nM and with a maximal occupancy of 348 fmol/mg protein. The correlation between .alpha.-adrenergic agonist or antagonist affinities for the membrane [<sup>3</sup>H]clonidine binding site with their physiol. potencies demonstrates the usefulness of the human fat cell as a model for investigating postsynaptic .alpha.2-adrenoceptor properties and regulation.  
 IT 67239-62-2  
 RL: BIOL (Biological study)  
 (adrenergic receptors of adipocyte cell membrane binding of, clonidine competition with)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinodione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1980:620771 CAPLUS  
 DOCUMENT NUMBER: 93:20771  
 TITLE: Fungicidal and bactericidal[4-(piperazin-1-ylphenyloxymethyl)-1,3-dioxolan-2-ylmethyl]-1H-imidazoles and -1H-1,2,4-triazole derivatives  
 INVENTOR(S): Heeres, Jan; Mostmans, Joseph  
 PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.  
 SOURCE: Eur. Pat. Appl., 68 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 6722	A1	19800109	EP 1979-301151	19790615
EP 6722	B1	19840905		
AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT 9227	E	19840916	AT 1979-301151	19790615
JP 62045389	B4	19880909	JP 1979-027239	19790702
US 4503055	A	19805035	US 1981-306267	19810928
PRIORITY APPLN. INFO.:			US 1976-921380	19760703
			US 1979-23807	19790326
			EP 1979-301151	19790615

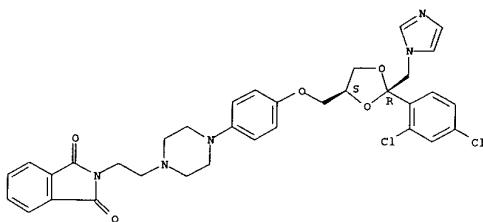
GI



AB Approx. 100 title compds. I ( $R = (\text{substituted}) \text{Ph}$ , thiienyl, or halothienyl;  $R_1 = \text{alkylsulfonyl}$ ,  $\text{CF}_3\text{SO}_2$ , alkyl or alkenyl substituted by  $\text{CN}_x$  ( $\text{substituted}) \text{NH}_2$ ,  $\text{N}$  heterocyclyl, aryl, or arylony, or  $R_1 = \text{C}(=\text{O})\text{R}_2\text{C}(=\text{O})\text{X}_1\text{R}_2$ , where  $\text{R}_2 = \text{H}$ , ( $\text{substituted}) \text{alkyl}$ , alkoxy, ( $\text{substituted}) \text{NH}_2$ , etc.,  $X_1 = \text{O}$  or  $S$ ,  $n = 0-6$ ;  $X = \text{CH}$  or  $\text{N}$ ) were prep'd. by several procedures. Thus, treatment of cis-1-[4-[(2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethoxy)-1,3-dioxolan-4-yl)methoxy]phenyl]piperazine with  $\text{ClCH}_2\text{CO}_2\text{Et}$  and  $\text{KCO}_3$  in  $\text{Me}_2\text{SO}$  gave cis-I ( $R = 2,4-\text{Cl}_2\text{C}_6\text{H}_3$ ,  $\text{R}_1 = \text{CO}_2\text{CH}_2\text{CO}_2\text{Et}$ ,  $X = \text{CH}$ ), which had ED<sub>50</sub> 2.5 mg/kg (p.o.) for vaginal candidosis in rats and ED<sub>50</sub> 31 mg/kg (in feed) for crop candidosis in turkeys.  
 IT 76049-34-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prep. and hydrolysis of)

L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RN 75049-24-0 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-{4-[(2-(2,4-dichlorophenyl)-1,3-dioxolan-4-yl)methoxy]phenyl}-1-piperazinyl]ethyl-, cis- (9CI) (CA INDEX NAME)

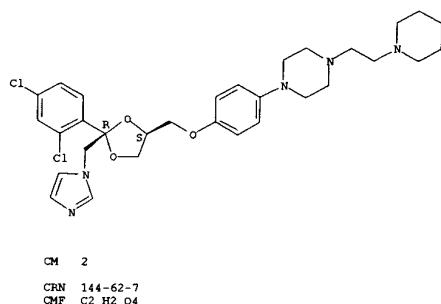
Relative stereochemistry.



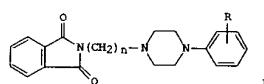
IT 75049-53-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)  
 RN 75049-53-5 CAPLUS  
 CN Piperazine,  
 1-[4-[(2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl)methoxy]phenyl]-4-[2-(1-piperidinyl)ethyl]-, cis-, ethanediolate (1:3) (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 75049-52-4  
 CMF C31 H39 Cl2 N5 O3  
 CDES 2:CIS

Relative stereochemistry.

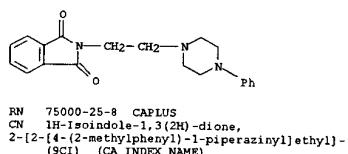
L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1980:1550208 CAPLUS  
 DOCUMENT NUMBER: 93:150208  
 TITLE: Synthesis and pharmacology of N-(N4-aryl-N1-piperazinylalkyl)phthalimides: CNS depressants  
 AUTHOR(S): Samant, S. D.; Kulkarni, R. A.  
 CORPORATE SOURCE: Chem. Dep., Ramnarain Ruia Coll., Bombay, 400 019,  
 India  
 SOURCE: J. Indian Chem. Soc. (1979), 56(10), 1002-5  
 CODEN: JICSAH; ISSN: 0019-4522  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

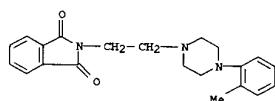


AB Twenty one phthalimides I ( $n = 1, 2, 3$ ;  $R = H, Me, Cl$ ) were prep'd. by Mannich reaction of phthalimides with piperazines in presence of  $HCHO$  or by reaction of bromoalkylphthalimides with arylpiperazines. These compounds were inactive as central nervous system depressants. I exhibited a tranquilizing effect on test animals and were non-toxic.  
 IT 75000-24-7P 75000-25-8P 75000-26-9P  
 75000-27-0P 75000-28-1P 75000-29-2P  
 75000-30-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. and tranquilizing activity of)  
 RN 75000-24-7 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

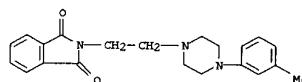


RN 75000-25-8 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

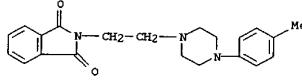
L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



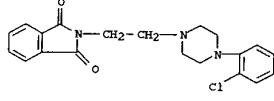
RN 75000-26-9 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(3-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



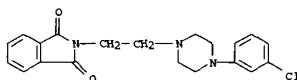
RN 75000-27-0 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(4-methylphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



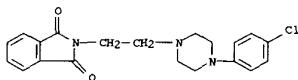
RN 75000-28-1 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



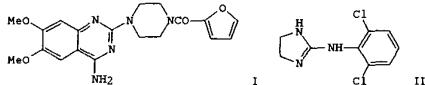
RN 75000-29-2 CAPLUS  
 CN 1H-Isoindole-1,3(2H)-dione,  
 2-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]-



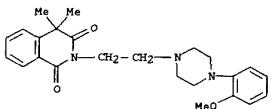
RN 75000-30-5 CAPLUS  
CN 1H-Isquinolone-1,3(2H)-dione,  
2-[2-(4-chlorophenyl)-1-piperazinyl]ethyl -  
(9CI) (CA INDEX NAME)



L14 ANSWER 236 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1980:525440 CAPLUS  
DOCUMENT NUMBER: 93:125440  
TITLE: 3H-Prazosin binds specifically to '.alpha.1'-  
adrenoceptors in rat brain  
AUTHOR(S): Miach, Peter J.; Dausse, Jean Pierre; Cardot,  
Alain;  
CORPORATE SOURCE: Meyer, Philippe  
SOURCE: Res. Unit. Hop. Necker, Paris, F-75015, Fr.  
312 (1), Naunyn-Schmiedeberg's Arch. Pharmacol. (1980),  
23-6  
DOCUMENT TYPE: CODEN: NSAPCC; ISSN: 0028-1298  
Journal  
LANGUAGE: English  
GI



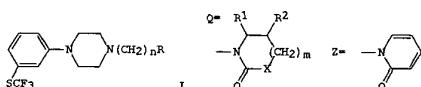
AB 3H-Labeled prazosin (I) [19216-56-9] was used to label biochemical studies of central alpha<sub>1</sub>-adrenoceptors. In rat brain membranes prazosin-3H bound specifically in a rapid, reversible and saturable manner to a single class of high affinity sites. The relative order of potencies for inhibition of prazosin-3H binding was WB4101 [2170-58-3] > ARC 239 [67339-62-2] > phentolamine [50-60-2] > yohimbine [146-48-5] which is a characteristic of the .alpha.1 type of adrenoceptors. In contrast, the relative order of potencies for inhibition of 3H-labeled clonidine (II) [4205-90-7] binding was yohimbine > piperoxane > WB4101 > ARC239 > prazosin which is a characteristic of the .alpha.2 type of adrenoceptors. Apparently, prazosin-3H binds to central .alpha.1-receptors and clonidine-3H binds to .alpha.2-receptors indicating the presence of two classes of .alpha.-adrenoceptors in rat brain membranes.  
IT 67339-62-2  
RL: BIOL (Biological study)  
(.alpha.1-.adrenergic receptors interaction with, in brain)  
RN 67339-62-2 CAPLUS  
CN 1,3(2H,4H)-Isoquinolinodione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1980:514564 CAPLUS  
DOCUMENT NUMBER: 93:114564  
TITLE: 1-Substituted alkyl-4-(3-trifluoromethylphenyl)piperazines  
INVENTOR(S): Majer, Henry; Manoury, Philippe; Kaplan, Jean Pierre  
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.  
SOURCE: Brit. UK Pat. Appl.: 7 pp.  
CODEN: BAXXDU  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2023594	A	19800103	GB 1979-21307	19790619
GB 2023594	B2	19821013		
FR 2429216	A1	19800118	FR 1978-18352	19780620
FR 2429216	A1	19800117		
FR 2429212	A1	19800118	FR 1978-18351	19780620
FR 2429212	B1	19801107		
CA 1124238	A1	19820525	CA 1979-329703	19790613
DK 7902510	A	19791221	DK 1979-2510	19790618
FI 7901926	A	19791221	FI 1979-1926	19790615
AU 7948112	A1	19800207	AU 1979-48112	19790615
AU 521110	B2	19820318		
US 4242343	A	19801230	US 1979-48814	19790615
NO 7902020	A	19791221	NO 1979-2020	19790618
ES 481632	A1	19800216	ES 1979-491632	19790618
BE 877099	A1	19800219	BE 1979-195839	19790619
SE 7505402	A	19791221	SE 1979-5402	19790619
DE 27391491	A1	19800110	DE 1979-329703	19790619
JP 55007274	A2	19800119	JP 1979-77489	19790619
ZA 7903070	A	19800730	ZA 1979-3070	19790620
PRIORITY APPLN. INFO.:				
			FR 1978-18351	19780620
			FR 1978-18352	19780620

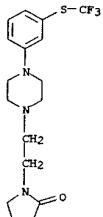
GI



AB The prepn. of the title compds. I [n = 1, 2, 3, R1 = Q (R1 = R2 = H, R1R2 = benzo; X = O, S, NH, alkylimino, CH2; m = 0, 1, Z, 2-tetrahydrofuryl, CH2SR3 (R3 = H, alkyl, acyl), Cl-alkoxymethyl] and 1 acid addn. salts is

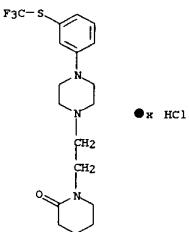
L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

Thus, I ( $n = 2$ , R = Q, R<sub>1</sub>R<sub>2</sub> = benzo, X = NMe, m = O) was prepd. by heating 4-(3-trifluoromethylthiophenyl)piperazine with K<sub>2</sub>CO<sub>3</sub>, KI, and 1-(.beta.-chloroethyl)-3-methylbenzimidazolidin-2-one in PhMe at reflux under N for 16 h. I are useful for the treatment of anxiety and of depression. Their activity was assessed orally in mice. LD<sub>50</sub> values for I in mice were 75-230 mg/kg for i.p. administration (48 h) and 250-1000 mg/kg for oral administration (7 days).  
 IT 74025-63-1P 74025-64-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (piperazine as tranquilizer and antidepressant)  
 RN 74025-63-1 CAPLUS  
 CN 2-Pyrolidine, 1-[2-[4-[3-((trifluoromethyl)thio)phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

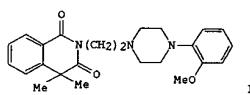


●x HCl  
 RN 74025-64-2 CAPLUS  
 CN 2-Piperidinone, 1-[2-[4-[3-((trifluoromethyl)thio)phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

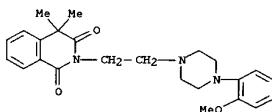


L14 ANSWER 238 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 ACCESSION NUMBER: 1980:437174 CAPLUS  
 DOCUMENT NUMBER: 93:37174  
 TITLE: Pharmacological properties of AR-C239,  
 2-[2-[4-(O-methoxyphenyl)-piperazine-1-yl]ethyl]4,4-dimethyl-1,3(2H,4H)-isoquinolinedione, a new .alpha.-adrenoceptor blocking drug  
 AUTHOR(S): Jacques, Mouille, Paule; Huchet, Anne Marie; Chelly, Lucet, Bernadette; Doursout, Marie Francoise; Schmitt, Henri  
 CORPORATE SOURCE: Dep. Pharmacol., Fac. Med., Paris, 75270/06, Fr.  
 SOURCE: J. Cardiovasc. Pharmacol. (1980), 2(2), 175-91  
 CODEN: JCPCDT; ISSN: 0160-2446  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB In pentobarbital-treated dogs and rats, AR-C239 (I) [67339-62-2] competitively antagonized pressor responses to adrenaline and inhibited pressor responses to noradrenaline, phenylephrine, tyramine, and dimethylphenylpiperazinium. Injected i.v. into closed-chest dogs, AR-C239 (3-50 .mu.g/kg) induced a progressive fall in blood pressure, heart rate, and sympathetic nerve activity. The drug appears to be devoid of direct vasodilator action, and the fall in blood pressure results from the peripheral .alpha.-blockade. AR-C239 did not change the tachycardia induced by stimulation of the cardiac nerve in dogs and, at least in this prepn., seems to be a specific .alpha.1-adrenoceptor blocking drug. When administered into the cisterna magna of dogs, AR-C239 did not have any centrally mediated cardiovascular actions and failed to block the inhibitor effects of clonidine on blood pressure and heart rate. AR-C239 did not have any centrally mediated cardiovascular actions and failed to block the inhibitory effects of clonidine on blood pressure and heart rate. AR-C239 did not modify the functioning of the baroreflex arc. Due

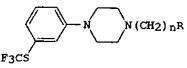
L14 ANSWER 238 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 for its specificity for .alpha.1-adrenoceptors, AR-C239 may be useful for characterizing .alpha.-adrenoceptors.  
 IT 67339-62-2  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmacol. of)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 239 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1980:426462 CAPLUS  
 DOCUMENT NUMBER: 93:26462  
 TITLE: Phenylpiperazine derivatives  
 PATENT ASSIGNEE(S): Synthelabo S. A., Fr.  
 SOURCE: *Neth. Appl.*, 9 pp.  
 CODEN: NAXXAN  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Dutch  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

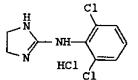
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 7904755	A	19791227	NL 1979-4755	19790619
FR 2429216	A1	19800118	FR 1978-18352	19780620
FR 2429216	B1	19801107		
FR 2429212	A1	19800118	FR 1978-18351	19780620
FR 2429212	B1	19801107		
CA 1124238	A1	19820525	CA 1979-329703	19790613
DK 7905210	A	19791221	DE 1979-2510	19790615
FI 1979-1926	A	19791221	FI 1979-1926	19790615
AU 7846112	A1	198001207	AU 1979-48112	19790615
AU 521110	B2	198001208		
US 4242343	A	198001230	US 1979-46814	19790615
NO 7902020	A	19791221	NO 1979-2020	19790618
ES 481632	A1	19800216	ES 1979-481632	19790618
BE 877099	A1	19791219	BE 1979-195839	19790619
SE 7905402	A	19791221	SE 1979-5402	19790619
DE 2924681	A1	19800110	DE 1979-2924681	19790619
JP 55007274	A2	19800119	JP 1979-77489	19790619
ZA 7903070	A	19800730	ZA 1979-3070	19790620
PRIORITY APPN. INFO.:			FR 1978-18351	19780620
			FR 1978-18352	19780620

GI



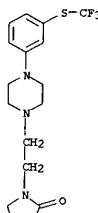
AB Tranquillizing (no data) piperazines I ( $n = 1-3$ ; R = heterocyclic amine) were prep'd. Thus, 4-(3-trifluoromethylthiophenyl)piperazine was treated with 1-(2-chloroethyl)-2-pyridone to give I ( $n = 2$ , R = 2-oxo-1-pyridyl).  
 IT 74025-63-1P 74025-64-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 74025-63-1 CAPLUS  
 2-Pyrrolidinone, 1-[2-[4-[(3-trifluoromethylthiophenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 240 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1980:174421 CAPLUS  
 DOCUMENT NUMBER: 92:174421  
 TITLE: Interactions between clonidine and .alpha.-adrenoceptor blocking drugs on the tachycardic response to stimulation of the cardiac nerve in dogs  
 AUTHOR(S): Mouille, Paule; Huchet, Anne Marie; Lucet, Bernadette;  
 CORPORATE SOURCE: Chelly, Jacques; Schmitt, Henri  
 SOURCE: Dep. Pharm., Fac. Med. Broussais, Paris, Fr.  
*J. Cardiovasc. Pharmacol.* (1979), 1(5), 515-28  
 CODEN: JCPCDT; ISSN: 0160-2446  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



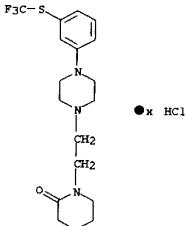
AB In pentobarbital-treated dogs clonidine-HCl (I) [4205-91-8] (10  $\mu$ M, g/kg) reduced the increase in heart rate caused by elec. stimulation of the cardiac nerve (1-10 Hz). Yohimbine-HCl [65-19-0] (0.3 mg/kg) and phentolamine-HCl [73-05-2] (1 mg/kg) potentiated the effects of nerve stimulation and antagonized the inhibitory effects of I. Piperoxan-HCl (135-87-5) (1 mg/kg) increased the response to nerve stimulation but antagonized the effects of I only at the lowest frequency of stimulation. Thymoxamine-HCl [964-52-3] (1 mg/kg) and prazosin-HCl [19237-84-4] at high doses (1 mg/kg) also antagonized the effects of I but failed to increase the pos. chronotropic response to stimulation of the cardiac nerve. AR-C239 [67339-62-2], a new and potent .alpha.-adrenoceptor blocking agent, changed neither the response to nerve stimulation nor the inhibitory effect of I. The effects of all these drugs were obse. at doses which reduced or reversed the pressor response to adrenaline. Therefore, the results afford further evidence for a dissimilarity between postsynaptic and presynaptic .alpha.-adrenoceptors in the dog. In addn., they show that the failure of an .alpha.-adrenoceptor blocking compd. to increase the response to nerve stimulation does not necessarily indicate a lack of presynaptic .alpha.-adrenoceptor blockade.

L14 ANSWER 239 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● x HCl

RN 74025-64-2 CAPLUS  
 2-Piperidinone, 1-[2-[4-[(3-trifluoromethylthiophenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

L14 ANSWER 240 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

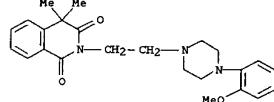
IT 67339-62-2 RL: BIOL (Biological study)

(heart response to clonidine in relation to)

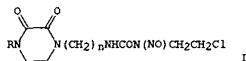
RN 67339-62-2 CAPLUS

1,3 (ZH,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-

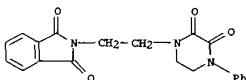
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



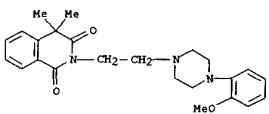
L14 ANSWER 241 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1979:611367 CAPLUS  
 DOCUMENT NUMBER: 91:211367  
 TITLE: Synthesis and physico-chemical properties of 1-(2-chloroethyl)-3-(4-substituted-2,3-dioxo-1-piperazinylalkyl)-1-nitrosoureas  
 AUTHOR(S): Hori, Takako; Momono, Kaishu; Kiba, Yasuo; Yoshida,  
 Chosaku; Sakai, Hiroshi; Takeno, Ryuko; Ohashi, Toshinori; Kishimoto, Sumikor; Saikawa, Isamu; Res. Lab., Toyama Chem. Co., Ltd., Toyama, Japan  
 CORPORATE SOURCE: YUKIZAJI, ISSN: 0031-6903  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese  
 GI



AB 1-(2-Chloroethyl)-3-(4-substituted-2,3-dioxo-1-piperazinylalkyl)-1-nitrosoureas I (R = H, Cl-8 alkyl, Ph; n = 0-6) were prep'd. by treating the dioxopiperazinylalkylamines with 4-02NC(H4O2CN)(NO)CH2CH2Cl on with ClCH2CH2NCO followed by nitrosation and their physico-chem. properties were exampd. Along with an increase in n, the alkylating activity was reduced, the stability in aq. soln. at pH 7-8 was increased, and the NH proton of the NMR spectrum was shifted to a higher field. These properties were not related to R.  
 IT 71999-88-7  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prep. and hydrazinolysis of)  
 RN 71999-88-7 CAPLUS  
 CN 1H-Isindole-1,3(2H)-dione, 2-(2,3-dioxo-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 242 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



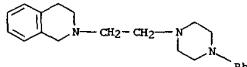
L14 ANSWER 242 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1979:115517 CAPLUS  
 DOCUMENT NUMBER: 90:115517  
 TITLE: Biochemical evidence for presynaptic and postsynaptic  $\alpha_1$ -adrenoceptors in rat heart membranes: Positive homotropic cooperativity of presynaptic binding  
 AUTHOR(S): Guichene, Pascale; Garay, Ricardo P.; Levy-Marchal, Claire; Meyer, Philippe  
 CORPORATE SOURCE: Dep. Physiol. Pharmacol., Hop. Necker, Paris, Fr.  
 SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1978), 75(12), 6285-9  
 CODEN: PNASAA; ISSN: 0027-8424  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In crude rat cardiac membrane preps., dihydroergocryptine-3H (I) appeared to bind 2 classes of sites with limited capacity, differing in their specificities and their affinities. The 1st class of binding sites interacted preferentially with the postsynaptic  $\alpha_1$ -adrenoceptor blocker ARC 239 (67339-62-2), as expected for postsynaptic  $\alpha_1$ -adrenoceptors. The binding of I to these receptors followed the law of mass action, with a high affinity for I apparent dissociation constant (Kd) at 25 degree. = 1.67 nM. Postsynaptic satg. levels of I were necessary to occupy the 2nd class of binding sites. These sites exhibited a preferential affinity for presynaptic ligands such as clonidine (4205-90-7) and yohimbine-HCl (65-19-0), as expected for presynaptic  $\alpha_1$ -adrenergic receptors. This presynaptic binding showed a markedly pos. homotropic cooperativity (Hill n = 2.88) with initial and final Kds of 23 and 0.83 nM, resp. Free energy of interaction between sites was of the order of 2 kcal (8.36 kJ)/mol of sites. These characteristics provide a rational mol. basis for the functional role of presynaptic  $\alpha_1$ -adrenoceptors that mediate the inhibition of norepinephrine release from nerve endings.  
 IT 67339-62-2  
 RL: PROC (Process)  
 (heart membrane binding of)  
 BN 67339-62-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 243 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1978:597598 CAPLUS  
 DOCUMENT NUMBER: 89:197598  
 TITLE: 1-Alkyl-substituted 4-phenylpiperazine derivatives  
 PATENT ASSIGNEE(S): MALESCI S.a.s. Istituto Farmacobiologico, Italy  
 SOURCE: Span., 29 pp.  
 CODEN: SPXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Spanish  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

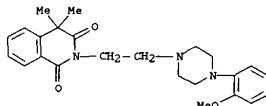
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 452530	A3	19780201	ES 1976-452530	19761019



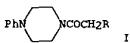
AB 1-Alkyl-4-arylpiperazines I (R = pyridyl, 4-imidazolyl, 1,2,3,4-tetrahydro-2-isoquinolyl, 1,2,3,4-tetrahydro-2-methyl-3-isoquinolyl; R1 = alkyl, R2 = H, Cl, F, Me, MeO) were prep'd. by treatment of ROCH2Br with 1-phenylpiperazine (II) or its aryl-substituted derivs., followed by redn. with NaBH4 and O-alkylation. Thus, III.HBr was treated with II in MeOH-Et3N under N at 5-10 degree. and then at room temp. The mixt. was cooled to 0 degree., aq. NaBH4 added dropwise and the mixt. kept at room temp. for 1 h. The product (I; R = 3-pyridyl, R1 = R2 = H) in HCCl3 at 0 degree. was treated with HCl (g), SOCl2 in HCCl3, and MeOH to give I (R = 3-pyridyl, R1 = Me, R2 = H).  
 IT 58013-22-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (prep. of)  
 RN 58013-22-2 CAPLUS  
 CN Isoquinoline, 1,2,3,4-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



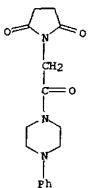
L14 ANSWER 244 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1978:500074 CAPLUS  
 DOCUMENT NUMBER: 89:100074  
 TITLE: Modifications of effects of cardiovascular nerve stimulation in the dog, by clonidine and several .alpha.-adrenolytics  
 AUTHOR(S): Bernadette, Mouille, Paule; Huchet, Anne-Marie; Lucet, Schmitt, Henri  
 CORPORATE SOURCE: Fac. med., Paris-Broussais-Hotel-Dieu, Paris, Fr.  
 SOURCE: C. R. Hebd. Seances Acad. Sci., Ser. D (1978), 286(19), 1399-402  
 CODEN: CHDDAT; ISSN: 0567-655X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: French  
 AB In anesthetized dogs clonidine [4205-90-7] (0.01mg/kg, i. v.) reduced the tachycardia induced by stimulation of the cardiac nerve at low frequencies. Small doses of yohimbine [146-48-5] (0.3mg/kg, i. v.) or piperoxan [59-39-2] (0.3 mg/kg, i. v.) increased the effects of nerve stimulation and in addn. antagonized the inhibitory effects of clonidine and reversed the pressor response to adrenaline [51-43-4].  
 Thymoxamine [54-32-0] (1 mg/kg, i. v.) and prazosin [19216-56-9] (1 mg/kg, i. v.) did not increase the effect of cardiac nerve stimulation, but reduced the effect of clonidine. ARC239 [67339-62-2] (0.05mg/kg-1) reversed the pressor response to adrenaline but even at high doses did not increase the effects of cardiac nerve stimulation or the effects of clonidine. Thus, pre- and post-synaptic .alpha.-adrenoceptors appear to be dissimilar.  
 IT 67339-62-2  
 RL: BIOL (Biological study)  
 (tachycardia from cardiac nerve stimulation response to, quantity in relation to)  
 RN 67339-62-2 CAPLUS  
 CN 1,3(ZH,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



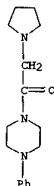
L14 ANSWER 245 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1978:50793 CAPLUS  
 DOCUMENT NUMBER: 88:50793  
 TITLE: Investigations on the piperazine series. New N-phenyl-piperazine acylate derivatives  
 AUTHOR(S): Zotta, V.; Popescu, Margareta; Missir, A.; Soare, Jean; Capitanescu, Victoria; Predescu, Viorica;  
 Dicu,  
 Elena; Neacsu, Maria  
 CORPORATE SOURCE: Lab. Chim. Farm., Fac. Farm., Bucharest, Rom.  
 SOURCE: Farmacia (Bucharest) (1977), 25(3), 129-35  
 CODEN: FRMBAZ  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Romanian  
 GI



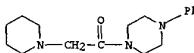
AB Nine piperazines I ( $R = 2,5\text{-dioxopiperidino}$ , piperidino, pyrrolidino, 2-pyridylamino, morpholino, etc.) were prep'd. by treating I ( $R = \text{Cl}$ ) with amines.  
 IT 65349-00-0P 65349-01-1P 65349-02-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep'n. of)  
 RN 65349-00-0 CAPLUS  
 CN Piperazine, 1-[(2,5-dioxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



RN 65349-01-1 CAPLUS  
 CN Piperazine, 1-phenyl-4-(1-pyrrolidinylacetyl)- (9CI) (CA INDEX NAME)

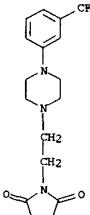


RN 65349-02-2 CAPLUS  
 CN Piperazine, 1-phenyl-4-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)



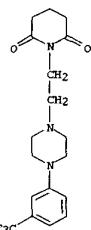
L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1977:495439 CAPLUS  
 DOCUMENT NUMBER: 87:95439  
 TITLE: Substituted trifluoromethyl phenyl piperazines as anorectic agents  
 AUTHOR(S): Cross, Peter E.; Dickinson, Roger P.; Halliwell, Geoffrey; Kemp, John E. G.  
 CORPORATE SOURCE: Pfizer Cent. Res., Pfizer Ltd., Sandwich/Kent, Engl.  
 SOURCE: Eur. J. Med. Chem. - Chim. Ther. (1977), 12(2), 173-6  
 CODEN: EJMCAS  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI For diagram(s), see printed CA issue.  
 AB In a series of trifluoromethyl phenyl piperazines possessing cyclo-imido alkyl side chains (I) several compds. possessed good anorectic activity with min. side effects on the central nervous system. The most potent was 1-(2-succinimidioethyl)-4-[4'-chloro-3-trifluoromethylphenyl]piperazine-HCl (II) [41213-05-2], which was prepd. by heating 1-[4'-chloro-3-(trifluoromethylphenyl)piperazine-HCl] [63556-37-6] with 2-succinimidioethyl chloride [41212-96-8] in dry dimethylformamide in the presence of base.  
 IT 41212-97-9P 41212-99-1P 41213-05-2P 63556-31-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. and anorexic activity of)  
 RN 41212-97-9 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 41212-99-1 CAPLUS  
 CN 2,6-Piperidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 41213-05-2 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-[4-chloro-3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

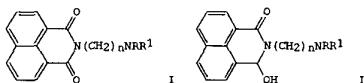
L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

● HCl  
  
 RN 63556-31-0 CAPLUS  
 CN 2-Pyrrolidinone, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 247 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1977:171284 CAPLUS  
 DOCUMENT NUMBER: 86:171284  
 TITLE: 2-[(Piperidinyl or tetrahydropyridinyl)-alkyl]-2,3-dihydro-3-hydroxy-1H-benz(de)isoquinolin-1-ones  
 INVENTOR(S): Wade, Peter C.; Vogt, Berthold Richard  
 PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA  
 SOURCE: U.S., 18 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4007191	A	19770208	US 1975-621939	19751014
GB 1567313		19800514	GB 1976-41959	19761008
CA 1068703	A1	19791224	CA 1976-263130	19761012
JP 52048674	A2	19770418	JP 1976-123369	19761014
DE 2646471	A1	19770421	DE 1976-2646471	19761014
FR 2327782	A1	19770513	FR 1976-30936	19761014
FR 2327782	B1	19781222		

PRIORITY APPLN. INFO.: US 1975-621939 19751014  
 GI

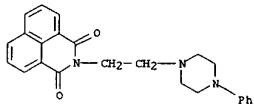


AB Benzisoquinolinediones I ( $n = 2-6$ , NR1 = 4-substituted 1,2,3,6-tetrahydropyridino, piperidino, piperazine) were prepd. by treating naphthalic anhydride with  $H_2N(CH_2)_nOH$ , tosylating, and treating the ester with HNR1 or by treating naphthalimide with  $Br(CH_2)_nBr$  and HNR1. I were reduced with NaBH4 to give II which have antidepressant activity (no data).

IT 58895-65-1  
 RL RCT (Reactant), SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. and redn. of)

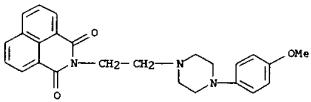
RN 58895-65-1 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione,  
 2-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

● HCl



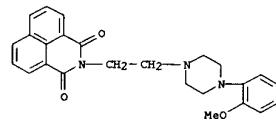
● 2 HCl

IT 58895-66-2P 58895-67-3P 58895-68-4P  
 58895-69-5P 58895-70-8P 58895-71-9P  
 58895-76-4P 58895-78-6P 62614-87-3P  
 RL SPN (Synthetic preparation); PREP (Preparation)  
 (prep., of)  
 RN 58895-66-2 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



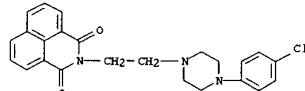
● 2 HCl

RN 58895-67-3 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



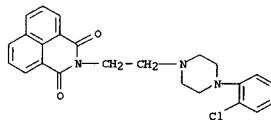
● 2 HCl

RN 58895-68-4 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

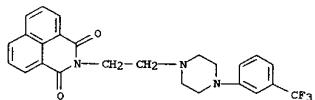


● HCl

RN 58895-69-5 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

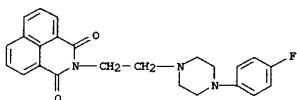


RN 58895-70-8 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione,  
 2-[2-[4-[3-(trifluoromethyl)phenyl]-  
 1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



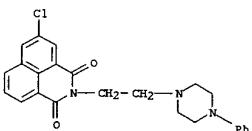
● HCl

RN 58895-71-9 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



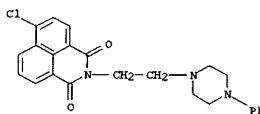
● HCl

RN 58895-76-4 CAPLUS  
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



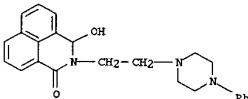
● HCl

RN 58895-78-6 CAPLUS



● HCl

RN 62614-87-3 CAPLUS  
 CN 1H-Benz[de]isoquinolin-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1976:150664 CAPLUS

DOCUMENT NUMBER: 84:150664

TITLE:

2-[1-(4-substituted-piperazinyl)alkyl]-1H-

benz[de]isoquinoline-1,3(2H)-diones

Wade, Peter C.; Vogt, Berthold R.

Squibb, E. R., and Sons, Inc., USA

SOURCE:

U.S., 8 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

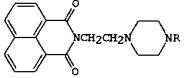
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3940367	A	19760224	US 1974-523293	19741113
CA 1058178	A1	19790710	CA 1975-239072	19751105
DE 2551062	A1	19760526	DE 1975-2551062	19751113
FR 2290903	A1	19760611	FR 1975-34615	19751113
FR 2290903	B1	19781110		
JP 51125293	A2	19761101	JP 1975-137115	19751113
PROPERTY APPLN. INFO.:			US 1974-523293	19741113
			US 1975-543558	19750123

GI



I

AB Benzisoquinolinediones (I, R = Ph, p-MeO-, o-MeOC<sub>6</sub>H<sub>4</sub>, p-Cl-, o-ClC<sub>6</sub>H<sub>4</sub>, m-F<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, p-FC<sub>6</sub>H<sub>4</sub>, PhCH<sub>2</sub>) were obtained as their hydrochlorides by treatment of naphthalic anhydride with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>OH to give a hydroxyethylbenzisoquinolinedione which was treated with p-MeC<sub>6</sub>H<sub>4</sub>-SO<sub>2</sub>Cl to give a sulfonate ester followed by treatment with the corresponding piperazine deriv. I were useful as antidepressants and inflammation inhibitors.

IT 58895-65-1P 58895-66-2P 58895-67-3P

58895-68-4P 58895-69-5P 58895-70-8P

58895-71-9P 58895-76-4P 58895-78-6P

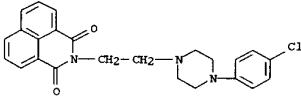
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 58895-65-1 CAPLUS

CN 1H-Benz[de]isoquinoline-1,3(2H)-dione,

2-[2-(4-phenyl-1-piperazinyl)ethyl]-,

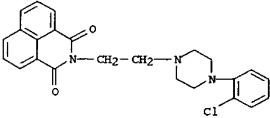
dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HC1

RN 58895-69-5 CAPLUS

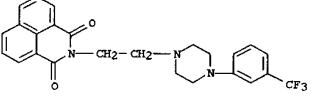
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 58895-70-8 CAPLUS

CN 1H-Benz[de]isoquinoline-1,3(2H)-dione,

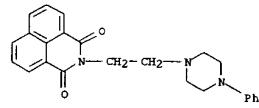
2-[2-[4-(3-trifluoromethylphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



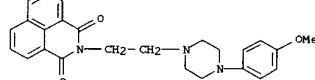
● HC1

RN 58895-71-9 CAPLUS

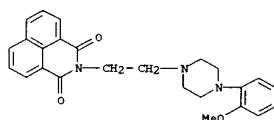
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



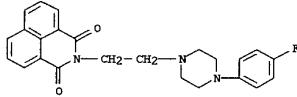
● 2 HC1

RN 58895-66-2 CAPLUS  
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

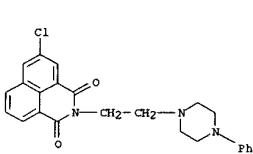
● 2 HC1

RN 58895-67-3 CAPLUS  
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

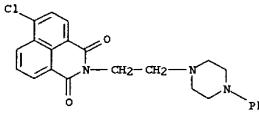
● 2 HC1

RN 58895-68-4 CAPLUS  
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-

● HC1

RN 58895-76-4 CAPLUS  
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-chloro-2-[2-[4-phenyl-1-

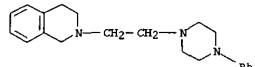
● HC1

RN 58895-78-6 CAPLUS  
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 6-chloro-2-[2-[4-phenyl-1-

● HC1

L14 ANSWER 249 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1976:59553 CAPLUS  
 DOCUMENT NUMBER: 84:59553  
 TITLE: Heterocyclic derivatives of substituted  
 1-alkyl-4-phenylpiperazine  
 INVENTOR(S): Giannini, Mario  
 PATENT ASSIGNEE(S): MALESCI S.a.s. Istituto Farmacobiologico, Italy  
 SOURCE: Beld., 31 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

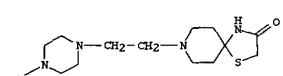
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 820242	A2	19750116	BE 1974-2053876	19740924
CH 624402	A	19810731	CH 1974-11406	19740821
			IT 1974-48923	19740301
PRIORITY APPLN. INFO.: IT 1974-48923 19740301				
GI For diagram(s), see printed CA Issue.				
AB Antihypertensive (no data) piperazines I were prep'd. Thus, I (R = 4-imidazoyl, R1 = H, R2 = H, 2-Me, 4-Me, 2-Cl, 2-OMe, 4-Cl, 4-OH, n = 0; R = 2-pyridyl(py), 3-py, 4-py, R1 = R2 = H, n = 0; R = 3-py, R1 = H, R2 = H, 2-OMe, 2-Cl, n = 1; R = 3-py, R1 = R2 = H, n = 2; R = 1,2,3,4-tetrahydro-2-isouinolyl, R1 = R2 = H, n = 1; R = 2-methyl-1,2,3,4-tetrahydro-3-isouinolyl, R1 = R2 = H, n = 0) were prep'd. by treating N-arylpiperazines (II) with R(CH <sub>2</sub> ) <sub>n</sub> Cl. I (R = 3-py, R1 = OH, R2 = H, 2-OMe, 3-OMe, 4-OH, 2-Me, 3-Me, 4-Me, 2-Cl, 3-Cl, 4-Cl, 2-F, n = 1; R = 4-py, R1 = OH, R2 = H, 2-OMe, n = 1) were prep'd. by treating II with RCOCH <sub>2</sub> Br and reducing the ketone in situ with NaBH <sub>4</sub> . I (R = 3-py, R1 = OMe, OEt, R2 = H, 2-OMe, 2-Cl, n = 1) were obtained by alkylating I (R1 = OH).				
IT 58013-22-2P RL SPT (Synthetic preparation); PREP (Preparation) (prep'n. of)				
RN 58013-22-2 CAPLUS CN Isouquinoline, 1,2,3,4-tetrahydro-2-(2-(4-phenyl-1-piperazinyl)ethyl)-(9CI) (CA INDEX NAME)				



L14 ANSWER 250 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1976:44001 CAPLUS  
 DOCUMENT NUMBER: 84:44001  
 TITLE: Spirocyclic compounds  
 INVENTOR(S): Nakashiba, Michio; Arimura, Katsuji; Tsing, In Mu  
 PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan  
 SOURCE: Japan., 4 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

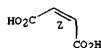
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49028195	B4	19740724	JP 1970-4618	19700117
GI For diagram(s), see printed CA Issue.				
AB Twenty-six thiadiazepiro compds. (I, n = 2, 3, R = Me, m-CF <sub>3</sub> CH <sub>4</sub> , p-ClCH <sub>3</sub> H <sub>4</sub> , etc., R1 = Me2N, Et2N, morpholino, H2N, 3-piperidinyl etc.) or their hydrochlorides or maleates, useful as antispasmodics, analgesics, and sedatives, (no data) were prep'd. by reacting the appropriate 1-(aminosalkyl)-4-piperidinone with HSCH <sub>2</sub> CO <sub>2</sub> H and (NH <sub>4</sub> ) <sub>2</sub> CO <sub>3</sub> (for I where R1 = H2N) or with PH. E.g., 18.4 g 1-(3-(dimethylamino)propyl)-4-oxopiperidine was refluxed with 14.5 g (NH <sub>4</sub> ) <sub>2</sub> CO <sub>3</sub> and 11 g HSCH <sub>2</sub> CO <sub>2</sub> H in 400 ml benzene for 15 hr to give 14 g I (n = 3, R = H, R1 = Me2N). cndot. 2HCl. II was prep'd. similarly.				
IT 54950-45-7P RL SPT (Synthetic preparation); PREP (Preparation) (prep'n. of)				
RN 54950-45-7 CAPLUS CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- , (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)				

CM 1  
 CRN 54950-44-6  
 CMF C19 H28 N4 O S



CM 2  
 CRN 110-16-7

Double bond geometry as shown.



L14 ANSWER 251 OF 263 CAPIUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1975:443207 CAPIUS  
 DOCUMENT NUMBER: 83:43207  
 TITLE: 2-(Piperazinylalkyl)isoquinolinediones  
 INVENTOR(S): Kutter, Eberhard; Austel, Volkhard; Eberlein,  
 Wolfgang; Heider, Joachim  
 PATENT ASSIGNEE(S): Linde AG  
 SOURCE: Ger. Offen., 23 pp.  
 CODEN: GWXMBX  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2345422	A1	19750320	DE 1973-2345422	19730908
DE 2345422	C2	19831222		
AT 1974-4	A	19761015		
AT 330777	B	19760726		
FI 7402465	A	19750309	FI 1974-2465	19740821
FI 52219	B	19770331		
ES 429473	A1	19760901	ES 1974-429473	19740823
US 3948898	A	19760406	US 1974-503072	19740904
SU 528035	D	19760905	SU 1974-2057995	19740904
AU 7473023	A1	19760311	AU 1974-73023	19740905
BE 819651	A1	19750306	BE 1974-148302	19740906
SE 7411312	A	19750310	SE 1974-11312	19740906
SE 424663	B	19820816		
SE 424663	C	19820816		
NO 1974-3220	A	19750311	NO 1974-3220	19740906
NO 140978	B	19780910		
NL 7411843	A	19750311	NL 1974-11843	19740906
NL 176363	B	19841101		
NL 176363	C	19850401		
FR 2242979	A1	19750404	FR 1974-30387	19740906
DK 7404727	A	19750505	DK 1974-4727	19740906
JP 50050381	A2	19750506	JP 1974-102862	19740906
JP 59006668	B4	19840215		
DD 115122	C	19750912	DD 1974-180966	19740906
HU 167869	F	19750225	HU 1974-T0040	19740906
ZA 4705688	A	19760165	ZA 1974-5688	19740906
GB 1974-7571	A	19760118	GB 1974-20093	19740906
CH 605778	A	19781013	CH 1974-12189	19740906
CH 605779	A	19781013	CH 1977-16014	19740906
RO 63655	P	19781015	RO 1974-79932	19740906
CS 185660	P	19781031	CS 1974-6150	19740906
PL 91712	Y	19770331	PL 1974-173958	19740907
ES 433959	A1	19761116	ES 1975-433959	19750120
ES 433958	A1	19761116	ES 1975-433958	19750120
SU 538664	D	19761205	SU 1975-2145942	19750620
SU 545256	D	19770130	SU 1975-2145935	19750620
AT 7505607	A	19750515	AT 1975-5607	19750721
AT 7575	B	19760110		
AT 7505606	A	19760115	AT 1975-5606	19750721
AT 334274	B	19760110		
US 4021558	A	19770503	US 1976-651568	19760122

L14 ANSWER 251 OF 263 CAPIUS COPYRIGHT 2002 ACS (Continued)  
 PRIORITY APPLN. INFO.: DE 1973-2345422 19730908  
 DE 1973-2345423 19730908  
 AT 1974-6514 19740808  
 US 1974-503072 19740904

GI For diagram(s), see printed CA issue.

AB Twenty-five isoquinolinediones I (R = Ph, substituted Ph, or 2-pyridyl; R1

or H; R2 = H, F, Cl, or MeO; n = 2 or 3), useful as antihypertensives or sedatives or in tachycardia treatment (no data), were prep'd. by reaction of the isochromandiones (II, X = O) or isoquinolinediones

II (X = NH) with (1-piperazinyl)alkylamines or (1-piperazinyl)alkyl chlorides, resp., or by reaction of the isoquinolinediones (II, X = N(CH2)nCl) with the piperazines.

IT 55974-36-2P 55974-37-3P 55974-38-4P

55974-38-4P 55974-40-6P 55974-42-0P

55974-42-1P 55974-43-3P 55974-44-9P

55974-47-5P 55974-48-6P 55974-49-7P

55974-51-1P 55974-52-2P 56010-74-3P

56045-26-2P

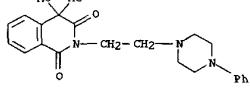
RL (SPN (synthetic preparation); PREP (Preparation)

(prep'n. of antihypertensive and sedative))

RN 55974-36-2 CAPLUS

1,3(2H,4H)-Isoquinolinedione, 7-chloro-4,4-dimethyl-2-[2-(4-phenyl-1-

piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

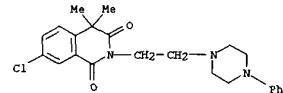


●2 HCl

RN 55974-37-3 CAPLUS  
 1,3(2H,4H)-Isoquinolinedione, 7-chloro-4,4-dimethyl-2-[2-(4-phenyl-1-

piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

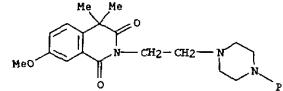
L14 ANSWER 251 OF 263 CAPIUS COPYRIGHT 2002 ACS (Continued)



●x HCl

RN 55974-38-4 CAPLUS  
 1,3(2H,4H)-Isoquinolinedione, 7-methoxy-4,4-dimethyl-2-[2-(4-phenyl-1-

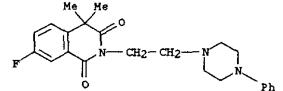
piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 55974-39-5 CAPLUS  
 1,3(2H,4H)-Isoquinolinedione, 7-fluoro-4,4-diphenyl-2-[2-(4-phenyl-1-

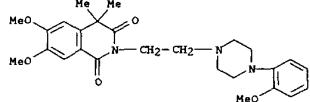
piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

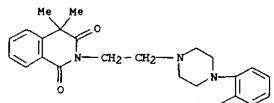
RN 55974-40-8 CAPLUS  
 1,3(2H,4H)-Isoquinolinedione,  
 6,7-dimethoxy-2-[2-(4-(2-methoxyphenyl)-1-

piperazinyl)ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



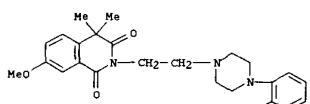
●x HCl

RN 55974-42-0 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



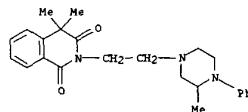
●2 HCl

RN 55974-43-1 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 7-methoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



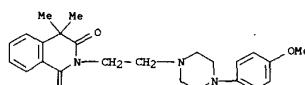
●2 HCl

RN 55974-45-3 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-(3-methyl-4-phenyl-1-



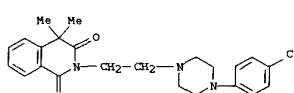
●2 HCl

RN 55974-46-4 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



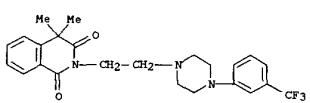
●2 HCl

RN 55974-47-5 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



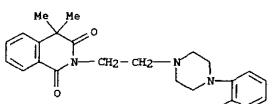
●2 HCl

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 55974-48-6 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[4-(3-trifluoromethyl)phenyl]-1-piperazinyl]ethyl-, hydrochloride (9CI) (CA INDEX NAME)



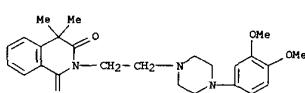
●x HCl

RN 55974-49-7 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



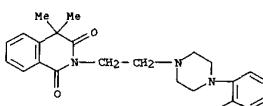
●x HCl

RN 55974-51-1 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(3,4-dimethoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



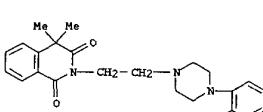
●2 HCl

RN 55974-52-2 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

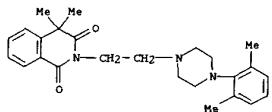
RN 56010-74-3 CAPLUS  
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-ethylphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 56045-26-2 CAPLUS

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 CN 1,3(2H,4H)-isoquinolinedione, 2-(2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

L14 ANSWER 252 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1975:410049 CAPLUS  
 DOCUMENT NUMBER: 83:10049  
 TITLE: Spirocyclic compounds  
 INVENTOR(S): Arimura, Katsuji Kohyagawa, Takahiro; Tsing, In  
 Mu;

Tsuda, Yoshiaki  
 Yoshitomi Pharmaceutical Industries, Ltd.  
 Jpn. Tokyo Koho, 4 pp.  
 CODEN: JAIXAD

DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

JP 45929196	B4	19740801	JP 1971-48716	19710702
CH 301634	A	19710115	CH 1968-501635	19680229
NL 6902779	A	19690902	NL 1969-2779	19690221
DK 122725	B	19720404	DK 1969-982	19690221
US 3624075	A	19711130	US 1969-801801	19690224
FR 2002897	A5	19691031	FR 1969-5170	19690227
BE 729209	A	19690828	BE 1969-729209	19690228
AT 286934	B	19710111	AT 1969-2034	19690228
AT 286997	B	19710111	AT 1970-2017	19690228
AT 286996	B	19710111	AT 1970-2014	19690228
ES 364635	A1	19710201	ES 1969-364635	19690228
ES 364633	A1	19710201	ES 1969-364633	19690228
ES 364637	A1	19710201	ES 1969-364637	19690228
ES 364634	A1	19710201	ES 1969-364634	19690228
ES 364632	A1	19710201	ES 1969-364632	19690228
AT 287729	B	19710210	AT 1970-2015	19690228
AT 289815	B	19710510	AT 1970-2016	19690228
GB 1259648	A	19720105	GB 1969-1259648	19690228
BR 6906750	A0	19730419	BR 1969-206750	19690228
JP 49027876	B4	19740722	JP 1969-14996	19690228
JP 49029197	B4	19740801	JP 1971-48717	19710702

PRIORITY APPLN. INFO.: CH 1968-3055 19680229

GI For diagram(s), see printed CA Issue.

AB Forty-three I [(R = Me2NCH2CH2, Me2N(CH2)3, Et2N(CH2)2, Et2N(CH2)3, 2-piperidinoethyl, 3-morpholinopropyl, etc.) R1 = H, Me, R2 = Ph, H, Et,

Et, CGH4CF3-*m*, CGH4Cl-*p*, etc.] or their salts, useful as analgesics and tranquilizers (no data), were prep'd. from RX (X = halogen) and I (R = H).

E.g., 7.6 g I (R = R1 = R2 = H). HBr in 80 ml DMF contg. 10 g Na2CO3 was heated at 80-95-degree. with 4.2 g Me2N(CH2)3Cl, the ppt. obtained dissolved in CHCl3 and washed with satd. sq. NaCl soln. to give 4 g I

(R = Me2N(CH2)3, R1 = R2 = H). cndot. 2HCl.

IT 54950-45-7P

RL SPN (Synthetic preparation); PREP (Preparation)

(preps. of)

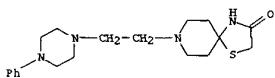
RN 54950-45-7 CAPLUS

CN 1-thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]-

L14 ANSWER 252 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 , (22)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

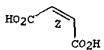
CRN 54950-44-6  
 CMF C19 H28 N4 O S



CM 2

CRN 110-16-7  
 CMF C4 H4 O4  
 CDES 2:Z

Double bond geometry as shown.



L14 ANSWER 253 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1974:505444 CAPLUS

DOCUMENT NUMBER: 81:105444  
 TITLE: Possible antiparkinsonian compounds. I.

Synthesis of N-aryl/alkyl-N'-phthalacyl glycyllid-alpha.-alpha.(-alanylpiperazines)

AUTHOR(S): Tiwari, S. S.; Pandey, V. K.

CORPORATE SOURCE: Dep. Chem., Lucknow Univ., Lucknow, India

SOURCE: Indian J. Appl. Chem. (1972), 35(4-6), 85-6

CODEN: JACAN

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB The piperazines I (R = Ph, p-MeC<sub>6</sub>H<sub>4</sub>, etc.; R1 = H, Me) were

prep'd. by treating phthaloylacyl chlorides with piperazines.

IT 53646-59-6P 53646-60-9P 53646-61-0P

53646-62-1P 53646-63-2P 53646-64-3P

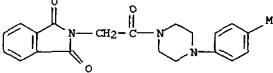
53646-65-4P 53646-66-5P

RL SPN (Synthetic preparation); PREP (Preparation)

(preps. of)

RN 53646-59-6 CAPLUS

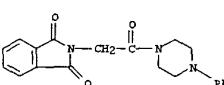
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isindol-2-yl)acetyl]-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 53646-60-9 CAPLUS

CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isindol-2-yl)acetyl]-4-phenyl-

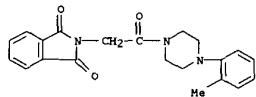
(9CI) (CA INDEX NAME)



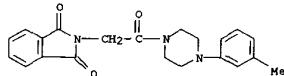
RN 53646-61-0 CAPLUS

CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isindol-2-yl)acetyl]-4-(2-

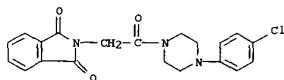
methylphenyl)- (9CI) (CA INDEX NAME)



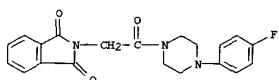
RN 53646-62-1 CAPLUS  
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



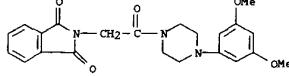
RN 53646-63-2 CAPLUS  
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]- (9CI) (CA INDEX NAME)



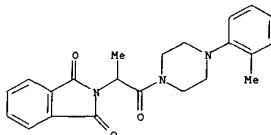
RN 53646-64-3 CAPLUS  
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 53646-65-4 CAPLUS  
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



RN 53646-66-5 CAPLUS  
CN Piperazine, 1-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxopropyl]- (2-methylphenyl)- (9CI) (CA INDEX NAME)



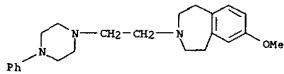
L14 ANSWER 254 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1574-82731 CAPLUS  
DOCUMENT NUMBER: 80:82731  
TITLE: 1,2,4,5-Tetrahydro-3H,3-benzazepines  
INVENTOR(S): Shetty, Bolu V.  
PATENT ASSIGNEE(S): Pennwalt Corp.  
SOURCE: Fr. Demande, 73 pp.  
CODEN: FRXXBL  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2171879	A1	19730928	FR 1972-4829	19720214
FR 2171879	B1	19750425		

G1 For diagram(s), see printed CA issue.

AB Benzazepines I (R = CH<sub>2</sub>CH<sub>2</sub>Me, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, allyl, 2-(4-phenylpiperazino)ethyl, CH<sub>2</sub>C(Me)CH<sub>2</sub>, CH<sub>2</sub>C(Me)CH<sub>2</sub>Ph, CH<sub>2</sub>CH<sub>2</sub>Ph, CH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>-p, CH<sub>2</sub>CH<sub>2</sub>OAc, CH<sub>2</sub>C(Me)OAc, CH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>-p) were prep'd. by substitution of I (R = H). I (R = H, R<sub>1</sub> = Me) was prep'd. by methylating 3,4-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>OH, oxidizing the 3,4-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>Me, converting the 4-MeOC<sub>6</sub>H<sub>4</sub>(CO<sub>2</sub>H)<sub>2</sub>-1,2 to its anhydride, reducing to 4-MeOC<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>Br)<sub>2</sub>-1,2, and converting to 4-MeOC<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>CN)<sub>2</sub>-1,2, which was cyclized to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine-2,4-dione and reduced with BH<sub>3</sub>. Demethylation with HBr gave I (R = R<sub>1</sub> = H). I are analgesics and narcotic antagonists. Thus, I (R = CH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>NHAc-p, R<sub>1</sub> = Me) had an oral ED<sub>50</sub> in the writhing test of 32 mg/kg.

IT 36134-36-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. cf)  
RN 36134-36-8 CAPLUS  
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- dihydrochloride (9CI) (CA INDEX NAME)



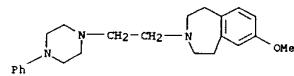
● 2 HCl

L14 ANSWER 255 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1973-526338 CAPLUS  
 DOCUMENT NUMBER: 79-126539  
 TITLE: 1,2,4,5-Tetrahydro-3H-3-benzazepines  
 INVENTOR(S): Shetty, Bala V.  
 PATENT ASSIGNEE(S): Pennval Corp.  
 SOURCE: Ger. Offen., 82 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

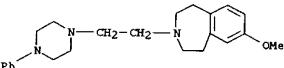
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2207430	A1	19730823	DE 1972-2207430	19720214
DE 2207430	B2	19810723		
DE 2207430	C3	19820513		

GI For diagram(s), see printed CA Issue.  
 AB Benzazepines I (R = H, CH<sub>2</sub>CH:CHMe<sub>2</sub>, CH<sub>2</sub>COMe:CH<sub>2</sub>, CH<sub>2</sub>CH:CHPh, allyl, CH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>Ph, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, trans-2-phenylcyclopropylmethyl, Me, Et, Pr, CH<sub>2</sub>CH<sub>2</sub>Ph, CHMeCH<sub>2</sub>Ph, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>-p, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NHAc-p, CH<sub>2</sub>CH<sub>2</sub>OAc, (CH<sub>2</sub>)<sub>3</sub>OAc, 4-phenylpiperazinyl ethyl, R1 = H, Me) were prep'd. Thus, 3,4-Me<sub>2</sub>CH<sub>3</sub>OH was methylated and oxidized to give 3,4-(HO<sub>2</sub>C)<sub>2</sub>CH<sub>3</sub>OMe, whose anhydride was reduced to 3,4-(HOCH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>OMe, brominated to 3,4-(BrCH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>OMe, treated with NaCN to give 3,4-(NCCH<sub>2</sub>)<sub>2</sub>CH<sub>3</sub>OMe, which was cyclized with HBr-HOAc to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine-2,4-dione and reduced with B2H<sub>6</sub> to I (R = H, R1 = Me) from which the other I were derived. I demonstrated antihistaminic, analgesic, anticholinergic, and morphine antagonist activity.  
 IT 36134-35-8P 36134-36-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 36134-35-7 CAPLUS  
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 255 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

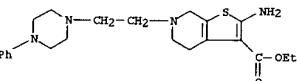


RN 36134-36-8 CAPLUS  
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 256 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1973-466340 CAPLUS  
 DOCUMENT NUMBER: 79-66340  
 TITLE: Aminocalkythienopyridine derivatives  
 INVENTOR(S): Nakanishi, Michio; Tahara, Tetsuji  
 PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd.  
 SOURCE: Jpn. Tokkyo Koho, 5 pp.  
 CODEN: JAXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 48015957	B4	19730518	JP 1969-104694	19691224

GI For diagram(s), see printed CA Issue.  
 AB The title derivs. I, useful as antiinflammatory and antidiuretic remedies, were prep'd. E.g., a mixt. of (2-(dimethylaminoethyl)-4-piperidone, CNCH<sub>2</sub>CO<sub>2</sub>E<sub>t</sub>, and S in EtOH was kept 1.5 hr at 60-70°, cooled, and (CO<sub>2</sub>H)<sub>2</sub> in EtOH added to give 63.2% I dioxalate (R = Me, R1 = EtCO<sub>2</sub>, n = 2). Similarly, the following I were prep'd. (R, R1, n given): piperidino, EtCO<sub>2</sub>, 3; pyrrolidino, EtCO<sub>2</sub>, 3; Et, EtCO<sub>2</sub>, 2; morpholino, NH<sub>2</sub>CO<sub>2</sub>, 2; EtCO<sub>2</sub>, 3; Et, CN, 2; morpholino, EtCO<sub>2</sub>, 2; 4-phenyl-1-piperazinyl, EtCO<sub>2</sub>, 2; piperidino, Et<sub>2</sub>, 3; and pyrrolidino, BuCO<sub>2</sub>, 3.  
 IT 42026-24-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 42026-24-4 CAPLUS  
 CN Thieno[2,3-c]pyridine-3-carboxylic acid, 2-amino-4,5,6,7-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

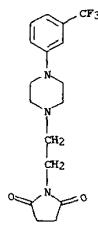


L14 ANSWER 257 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1973-159666 CAPLUS  
 DOCUMENT NUMBER: 78-159666  
 TITLE: Anorexigenic 1-ethyl-4-[m-(trifluoromethyl)phenyl]piperazine derivatives  
 INVENTOR(S): Pfizer Corp.  
 PATENT ASSIGNEE(S): Pfizer Corp.  
 SOURCE: Ger. Offen., 27 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2242328	A1	19730215	DE 1972-2242382	19720829
AU 7245940	A1	19740226	AU 1972-45940	19720824
NL 72211694	A	19730306	NL 1972-121694	19720828
BE 788280	A1	19730228	BE 1972-121582	19720828
FR 2154449	A1	19730511	FR 1972-31080	19720901
CH 551430	A	19740715	CH 1974-3568	19720901
CH 554899	A	19741015	CH 1972-12935	19720901
AT 320655	B	19750225	AT 1973-10899	19720901
AT 321307	B	19750325	AT 1972-7520	19720901
ES 4080584	A2	19731113	JP 1972-88020	19720904
ES 406374	A1	19750716	ES 1972-406374	19720904

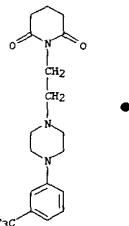
PRIORITY APPLN. INFO.: GB 1971-41322 19710904  
 GB 1972-20536 19720503

GI For diagram(s), see printed CA Issue.  
 AB Eight title compds. (I, R = H, Cl, or Br; R1 = e.g. succinimido, glutarimido, or 2,4-dioxo-3-imidazolidinyl) and (or) their HCl salts were prep'd. and used as appetite depressants. Thus, 11.5 g 1-[m-(trifluoromethyl)-phenyl]piperazine, 8.1 g .beta.-succinimidoethyl chloride, K<sub>2</sub>CO<sub>3</sub>, and MeI were heated in DMF for 24 hr at 100° to give 9.1 g I-HCl (R = H, R1 = succinimido).  
 IT 41212-97-9P 41212-99-1P 41213-05-2P  
 41213-07-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 41212-97-9 CAPLUS  
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



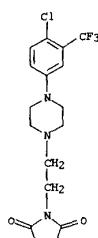
● HCl

RN 41212-99-1 CAPLUS  
CN 2,6-Piperidinedione, 1-[2-[4-(3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



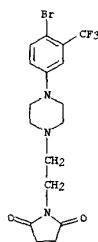
● HCl

RN 41213-05-2 CAPLUS  
CN 2,5-Pyrrolidinedione, 1-[2-[4-(4-chloro-3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

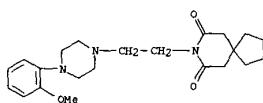


● HCl

RN 41213-07-4 CAPLUS  
CN 2,5-Pyrrolidinedione, 1-[2-[4-(4-bromo-3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



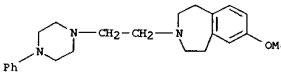
L14 ANSWER 258 OF 263 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1972:443062 CAPLUS  
DOCUMENT NUMBER: 77:43062  
TITLE: Psychosedative agents. 2. 8-(4-Substituted 1-piperazinylalkyl)-8-azaspiro[4.5]decano-7,9-diones  
AUTHOR(S): Wu, Yao-Hua; Rayburn, J. W.; Allen, L. E.; Ferguson, H. C.; Kissel, J. W.  
CORPORATE SOURCE: Dep. Chem. Res., Mead Johnson Res. Cent., Evansville, Indiana, USA  
SOURCE: J. Med. Chem. (1972), 15(5), 477-9  
CODEN: JMCMAR  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Several of the title compds. synthesized had greater potency and selectivity as tranquilizers than chlorpromazine [50-53-3]. Thus, 2-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decano-7,9-dione (I) [33386-08-2] had an ED50 for complete suppression of conditioned avoidance response of 4.3 mg/kg i.p. in rats; 19.6 times this dose was required for complete suppression of the unconditioned escape response. Corresponding data for the 2-pyridyl analog and chlorpromazine were 2.8 and 4.8 mg/kg, and 12.1 and 10.2 times, resp. I produced much less sedation than chlorpromazine, had very little .alpha.-adrenergic blocking activity in vivo and in vitro, and had an LD50 of 146 mg/kg i.p. in mice. The incidence of catalepsy induced by I in monkeys was similar to that with chlorpromazine. To synthesize I, N-(2-pyrimidinyl)piperazine was prep'd. from piperazine and 2-chloropyrimidine by nucleophilic aromatic substitution, reacted with .omega.-chloropropionitrile, reduced with LiAlH<sub>4</sub> or Raney Ni-H<sub>2</sub> to 1-(.omega.-aminoethyl)-4-(2-pyrimidinyl)piperazine, and reacted with the spiro compd. cyclopentane-1,1-diacetic acid anhydride.  
IT 21102-95-0  
RN 21102-95-0 Biological activity or effector, except adverse; BIOL (Biological study)  
(tranquillizing activity of)  
RN 21102-95-4 CAPLUS  
CN 8-Azaspiro[4.5]decano-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 259 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1972:153628 CAPLUS  
 DOCUMENT NUMBER: 76:153628  
 TITLE: 1,2,4,5-Tetrahydro-3H-3-benzazepines as  
 analgesics and  
 antagonists of narcotics  
 PATENT ASSIGNEE(S): Wallace and Tiernan, Inc.  
 SOURCE: Brit., 42 pp.  
 CODEN: BRKGAA  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

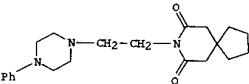
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1268243		19720322		
PRIORITY APPLN. INFO.: US 1968-711897 19680311				
GI For diagram(s), see printed CA Issue.				
AB H-3-Benzazepines (I, R was usually 7- or 8-MeO or 7-OH; R1 was, e.g., H, phenyl, cycloalkylmethyl, substituted phenethyl, p-MeC <sub>6</sub> H <sub>4</sub> S0 <sub>2</sub> , a cetoxyalkyl; R <sub>2</sub> = H3 Me), useful as analgesics, anticholinergics, antihistamines, and antagonists to narcotics, were prep'd. Thus, 50 g 4-methoxy-.omega.-methylene-.alpha.,.alpha.-dihydro-4-methoxy-1H-3-benzazepine (II) was reduced by borane in THF at 10.degree. to give 28 g I (R = 7-MeO, R <sub>1</sub> = R <sub>2</sub> = H), analyzed as the maleate. II was prep'd. from 3,4-dimethylphenol by methylation, oxidn. to 4-methoxyphthalic acid, formation of the anhydride, redn. to 4-methoxy-.omega.-methylene-.alpha.,.alpha.-diol, dibromination of the diol, conversion to the dinitrile, and cyclization to the imide. Pharmacol. test results were given.				
IT 36134-35-7P 36134-36-8P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)				
RN 36134-35-7 CAPLUS CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)				



RN 36134-36-8 CAPLUS  
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

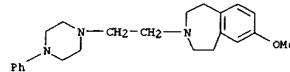
L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1971:125435 CAPLUS  
 DOCUMENT NUMBER: 74:125435  
 TITLE: Pharmacologic compositions containing  
 azaspirodecanediones and azaspirodecanediones  
 INVENTOR(S): Wu, Tao Hua  
 PATENT ASSIGNEE(S): Mead Johnson and Co.  
 SOURCE: U.S., 6 pp. Continuation-in-part of U.S.  
 3,398,151  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3550777	A	19710126	US 1968-738848	19680621
AB The disclosure is similar, but the claims are different.				
IT 21090-08-4P 21102-95-4P 21102-99-8P 25024-82-2P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)				
RN 21090-08-4 CAPLUS CN 1,1-Cyclopentanediacetimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)				



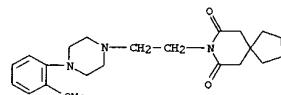
● HCl  
 RN 21102-95-4 CAPLUS  
 CN 1,1-Cyclopentanediacetimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



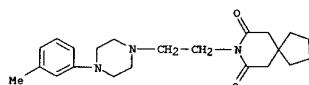
● 2 HCl

L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

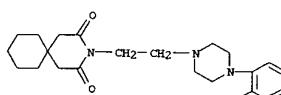


● HCl

RN 21102-99-8 CAPLUS  
 CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl  
 RN 25024-02-2 CAPLUS  
 CN 1,1-Cyclohexanediacetimide, N-[2-(4-(o-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

FSI.J51.

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1969:500204 CAPLUS  
 DOCUMENT NUMBER: 71:100204  
 TITLE: Psychoactive agents. N-(4-phenyl-1-piperazinylalkyl)-substituted cyclic imides  
 AUTHOR(S): Wu, Yao-Hua; Smith, Kenneth R.; Rayburn, James W.  
 CORPORATE SOURCE: Kissel, John W.  
 Evansville, Dep. Pharmacol., Head Johnson Res. Center,  
 Indiana, USA

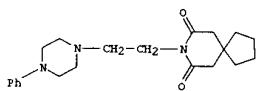
SOURCE: J. Med. Chem. (1969), 12, 876-81  
 CODEN: JMCHAR  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Fifty-two N-substituted cyclic imides bearing a 4-phenyl-1-piperazinylalkyl moiety were synthesized and screened as psychoactive agents. The results of 2 test methods, (a) antagonism of amphetamine-aggregation stages in mice, and (b) suppression of the conditioned avoidance response in rats, indicate that these compds. possess in varying degrees psychotropic properties typical of major tranquilizers.

IT 21090-08-4 21102-95-4 21102-99-8  
 21103-15-1 21103-17-3 21103-21-9  
 21103-24-2 25024-54-8 25024-66-2  
 25024-74-2 25024-76-4 25024-82-2  
 25024-84-4 25024-90-2 25024-91-3  
 25024-92-4 25024-93-5 25024-94-6  
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study); TRA (Tranquillizing activity of)

RN 21090-08-4 CAPLUS

CN 1,1-Cyclopentanediacetimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

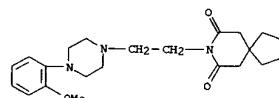


● HCl

RN 21102-95-4 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

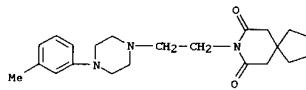
L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● 2 HCl

RN 21102-99-8 CAPLUS

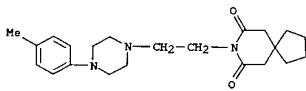
CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 21103-15-1 CAPLUS

CN 1,1-Cyclopentanediacetimide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)

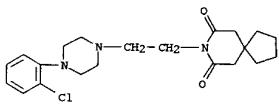


● 2 HCl

RN 21103-17-3 CAPLUS

CN 1,1-Cyclopentanediacetimide, N-[2-(4-(o-chlorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

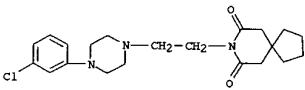
L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 21103-21-9 CAPLUS

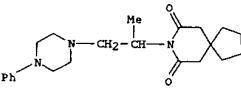
CN 1,1-Cyclopentanediacetimide, N-[2-(4-(m-chlorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 21103-24-2 CAPLUS

CN 1,1-Cyclopentanediacetimide, N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)

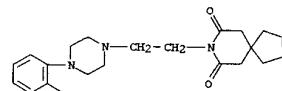


● 2 HCl

RN 25024-54-8 CAPLUS

CN 1,1-Cyclopentanediacetimide, N-[2-(4-o-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

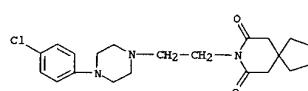
L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 25024-66-2 CAPLUS

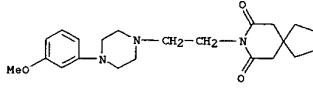
CN 1,1-Cyclopentanediacetimide, N-[2-(4-(p-chlorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 25024-74-2 CAPLUS

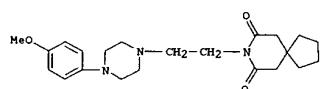
CN 1,1-Cyclopentanediacetimide, N-[2-(4-(m-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

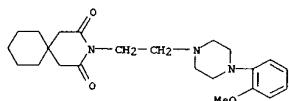
RN 25024-76-4 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



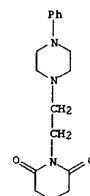
● HCl

RN 25024-82-2 CAPLUS  
 CN 1,1-Cyclohexanedicetamide,  
 N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-  
 , monohydrochloride (8CI) (CA INDEX NAME)



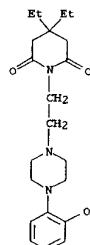
● HCl

RN 25024-84-4 CAPLUS  
 CN Glutarimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride  
 (8CI) (CA INDEX NAME)



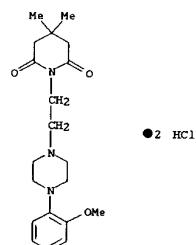
● HCl

RN 25024-90-2 CAPLUS  
 CN Glutarimide,  
 3,3-diethyl-N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-,  
 monohydrochloride (8CI) (CA INDEX NAME)



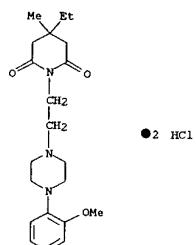
● HCl

RN 25024-91-3 CAPLUS  
 CN Glutarimide,  
 N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-dimethyl-,  
 dihydrochloride (8CI) (CA INDEX NAME)



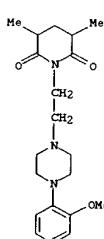
● 2 HCl

RN 25024-92-4 CAPLUS  
 CN Glutarimide,  
 3-ethyl-N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-3-  
 methyl-, dihydrochloride (8CI) (CA INDEX NAME)

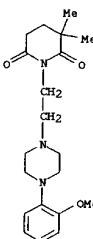


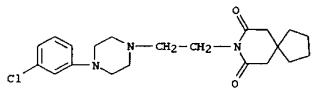
● 2 HCl

RN 25024-93-5 CAPLUS  
 CN 2,6-Piperidinedione,  
 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,5-  
 dimethyl- (9CI) (CA INDEX NAME)



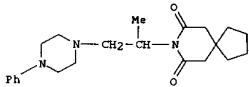
RN 25024-94-6 CAPLUS  
 CN 2,6-Piperidinedione,  
 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-  
 dimethyl- (9CI) (CA INDEX NAME)



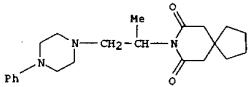


● HCl

RN 21103-23-1 CAPLUS  
 CN 1,1-Cyclopentanediacetimide,  
 N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-  
 (8CI) (CA INDEX NAME)



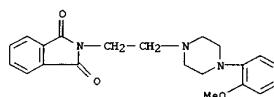
RN 21103-24-2 CAPLUS  
 CN 1,1-Cyclopentanediacetimide,  
 N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-  
 dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 263 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1968:410474 CAPLUS  
 DOCUMENT NUMBER: 69:10474  
 TITLE: Preparation of phthalimidoalkyl piperazines  
 INVENTOR(S): Lovrinovics, E.; Grinstein, V.  
 SOURCE: U.S.S.R.  
 CODEN: URXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Russian  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 193524		19670313	SU	19660407
AB	From Izobret., Prom. Obratsey, Tovarnye Znaki 1967, 44(7), 39.			
	N-alkylpiperazine is treated with N-haloalkylphthalimide in MeOH under reflux to yield the title compds.			
IT 18502-07-6*				
PL SPN (Synthetic preparation); PREP (Preparation) (prep. of)				
RN 18503-07-6 CAPLUS				
CN Phthalimide, N-[4-(o-methoxyphenyl)-1-piperazinyl]methyl]- monohydrobromide (8CI) (CA INDEX NAME)				



● HBr

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1969:4143 CAPLUS  
 DOCUMENT NUMBER: 70:4143  
 TITLE: Azaspirodecanediones and azaspiroundecanediones  
 INVENTOR(S): Wu, Yao Hua  
 PATENT ASSIGNEE(S): Head Johnson and Co.  
 SOURCE: U.S., 8 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

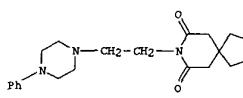
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3398151	A	19680820	US 1967-607908	19670109

GI For diagram(s), see printed CA Issue.  
 AB 8-(4-Phenyl-1-piperazinylalkylene)-8-azaspiro[4.5]decane-7,9-diones (I, A = (CH<sub>2</sub>)<sub>x</sub>) having 0-3 substituents in the Ph ring were synthesized from the corresponding 4-phenylpiperazines and 3,3-tetramethylene glutaric anhydride (II). Employing 3,3-pentamethylene glutaric anhydride in the method yielded the 3-azaspiro[5.5]undecane-2,4-dione analog. These substances have strong activity and good selectivity in suppressing conditioned avoidance response in animals and are useful as psychotropic agents, analgesics, centrally acting muscle relaxants, capillary protectants, antiallergic agents, anti-inflammatory agents, and antiemetics. Thus, a mixt. of 0.1 mole of the substituted glutaric anhydride, 0.1 mole 1-(*o*-methylalkyl)-4-phenylpiperazine, and 400 ml. C<sub>6</sub>H<sub>5</sub>N was refluxed 15 hrs., the solvent distd., and the residue purified by distn. in vacuo or crystn. If the residue contained amide and carboxyl bands in the ir, it was refluxed with 10 parts by wt. Ac<sub>2</sub>O for 15 hrs. prior to purification as above. The HCl salt of the free base was prep'd. by treating the EtOH soln. of the free base with an equiv. amt. of ethanolic HCl soln. The following I were thus obtained (n A, R, b.p./mm.)  
 1 yield, m.p. of HCl salt, and crystn. solution given: 4, (CH<sub>2</sub>)<sub>2</sub>, H 215-35.degree./0.45, 80, 135-7.degree. (decompn.), iso-PrOH 4, (CH<sub>2</sub>)<sub>3</sub>, H, 250-2.degree./0.5, 80, 234.5-6.5.degree. (decompn.), iso-PrOH-EtOH; 4, (CH<sub>2</sub>)<sub>4</sub>, H, 260-75.degree./0.1, 82.8, 218.5-20.5.degree. (decompn.), iso-PrOH 4, (CH<sub>2</sub>)<sub>5</sub>, H, 253-63.degree./0.2, 89, 188.5-96.5, EtOH; (CH<sub>2</sub>)<sub>3</sub>, H, 263-76.degree./0.15-0.25, 77.6, 254-5.degree. (decompn.). EtOH, 5, (CH<sub>2</sub>)<sub>2</sub>, o-Me, 230-60.degree./0.2, 92, 211-12.degree. (decompn.), EtOH; 4, (CH<sub>2</sub>)<sub>2</sub>, o-Me (III), 220-40.degree./0.35, 77, 196.5-8.5.degree.

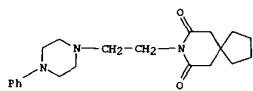
L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (decompn.), EtOH); 4, (CH<sub>2</sub>)<sub>3</sub>, o-Me, 220-50.degree./0.11, 90, 208-10.5-degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>2</sub>, m-Me, 225-35.degree./0.3, 81, 205.5-7.0.degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>3</sub>, o-Cl, 215-45.degree./0.1, 94, 234.5-5.5.degree. (decompn.), iso-PrOH; EtOH; 4, (CH<sub>2</sub>)<sub>2</sub>CHMeCH<sub>2</sub>, H, 235-50.degree./0.25, 80, 207.5-12.0.degree., iso-PrOH; 4, (CH<sub>2</sub>)<sub>4</sub>, o-Me, 243-7.degree./0.18, 89.6, 199.5-203.degree., EtOH; 4, (CH<sub>2</sub>)<sub>3</sub>, o-Cl, 240-60.degree./0.2, 90, 238.5-41.0.degree., EtOH; 4, (CH<sub>2</sub>)<sub>4</sub>, o-Me, 230-70.degree./0.1, 95, 202-3.5.degree., EtOH; 4, (CH<sub>2</sub>)<sub>5</sub>, o-Me, 255.degree./0.01, 86, 246-7.5.degree., EtOH; 4, (CH<sub>2</sub>)<sub>3</sub>, o-Me, 230-50.degree./0.3, 90, 254.5-5.5.degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>3</sub>, o-Me, -88, 174.5-6.5.degree., EtOH-Et<sub>2</sub>O; 4, (CH<sub>2</sub>)<sub>3</sub>, p-Me, 160-80.degree./0.1, 75, 247-8.degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>2</sub>, o-Cl, 165-84.degree./0.1, 80, 241-2.5.degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>3</sub>, p-Cl, 164-70.degree./0.1, 68, 248.5-50.5.degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>2</sub>, m-Cl, 140-210.degree./0.5-0.1, 74, 226.5-8.5.degree. (decompn.), iso-PrOH; 4, (CH<sub>2</sub>)<sub>3</sub>, p-Cl, 175-97.degree./0.1, 90, 248-9.degree. (decompn.), EtOH; 4, CH<sub>2</sub>CH<sub>2</sub>, H, 230-40.degree./0.25, 87, 255.5-7.5.degree., EtOH. A stirr. mixt. of 19.2 g. 1-(*o*-methoxyphenyl)-piperazine (IV), 9.0 g. ClCH<sub>2</sub>CH<sub>2</sub>CN, 150 ml. C<sub>6</sub>H<sub>6</sub>, and 16.6 g. anhyd. Na<sub>2</sub>CO<sub>3</sub> was refluxed overnight under anhyd. conditions and filtered, the filter cake washed with C<sub>6</sub>H<sub>6</sub>, and the combined C<sub>6</sub>H<sub>6</sub> filtrates fractionally distd. in vacuo to give 19.6 g. 1-(2-cyanoethyl)-4-(*o*-methoxyphenyl)piperazine (V), b1 208-26.degree., m. 72-4.degree.. A mixt. of 8.1 g. V, 30 g. dry liq. NH<sub>3</sub>, and 100 ml. abs. MeOH was hydrogenated at 1200 psi. and room temp. over W-6 Raney Ni to give 85% 1-(3-aminopropyl)-4-(*o*-methoxyphenyl)piperazine (VI, A = (CH<sub>2</sub>)<sub>3</sub>, R, = o-Me). The following VI were similarly prep'd. (except that the last five compds. were prep'd. by redn. with LiAlH<sub>4</sub>, an example of which is given below) (A, R, % yield, b.p./mm., and n<sub>D</sub><sup>25</sup> given): (CH<sub>2</sub>)<sub>2</sub>, m-Me, 85, 5, 117-34.degree./0.3, 1.5638; (CH<sub>2</sub>)<sub>3</sub>, m-Me, 68, 8, 115-65.degree./0.1, 1.5561; (CH<sub>2</sub>)<sub>3</sub>, m-Me, 48.0, 120.degree./0.18, 1.5656; (CH<sub>2</sub>)<sub>3</sub>, m-Cl, 79, 142-70.degree./0.15-0.5, -1, (CH<sub>2</sub>)<sub>3</sub>, m-Cl, 62, 108-40.degree./0.1-0.15, 1.5827; (CH<sub>2</sub>)<sub>2</sub>CNMe<sub>2</sub>, H, 81.7, 138-55.degree./0.1, 1.5465; (CH<sub>2</sub>)<sub>3</sub>, m-Cl, 78.6, 150-50.degree./0.25, 1.5560; (CH<sub>2</sub>)<sub>4</sub>, 1.5496; (CH<sub>2</sub>)<sub>4</sub>, o-Cl, 74.0, 130-65.degree./0.15-0.3, 1.5560; (CH<sub>2</sub>)<sub>4</sub>, o-Me, 32.8, 145-60.degree./0.08, -1, (CH<sub>2</sub>)<sub>5</sub>, o-Me, 57.6, 163-72.degree./0.2, 1.5444; 1-(3-Cyano-2-methylpropyl)-4-

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 phenylpiperazine, b0.15 155-68.degree., m. 81-3.degree., prep'd. in 65% yield from 3-chloro-2-methylbutyronitrile by the above procedure, was dissolved (0.04 mole) in 100 ml. tetrahydrofuran, the soln. added dropwise with vigorous stirring during 35 min. to a suspension of 1.87 g. LiAlH<sub>4</sub> in 100 ml. Et<sub>2</sub>O and refluxed, and the residue distd. in vacuo to give 81.7% 1-(4-amino-2-methylbutyl)-4-phenylpiperazine, b0.17 138-55.degree., n<sub>D</sub><sup>25</sup> 1.5485. A stirred mixt. of 16.8 g. II and 200 ml. C<sub>6</sub>H<sub>5</sub>N was treated with 12.2 g. ethanalamine, refluxed 3 hrs., and fractionally distd. in vacuo to give 12.0 g. 8-(2-hydroxyethyl)-8-azaspiro[4.5]decane-7,9-dione [VII, A = (CH<sub>2</sub>)<sub>2</sub>, X = OH] (VIIa), b0.05-0.1 142-50.degree., n<sub>D</sub><sup>25</sup> 1.5150. A cooled mixt. (10-15.degree.) of 6.0 g. VIIa, 50 ml. C<sub>6</sub>H<sub>6</sub>, and 2.4 g. C<sub>6</sub>H<sub>5</sub>N was treated dropwise during 25 min. with 3.6 g. SOC<sub>12</sub>, heated 1 hr. at 60-5.degree., and filtered, the filtrate treated with 20 ml. distd. H<sub>2</sub>O, and the C<sub>6</sub>H<sub>6</sub> layer sepd., dried, and fractionally distd. in vacuo to give 4.5 g. 8-(2-chloroethyl)-8-azaspiro[4.5]decane-7,9-dione [VII, A = (CH<sub>2</sub>)<sub>2</sub>, X = Cl] (VIIb), b0.05 120-2.degree., n<sub>D</sub><sup>25</sup> 1.5139. The following VII were similarly prep'd. (A, X, b.p./mm., and % yield given); (CH<sub>2</sub>)<sub>3</sub>, OH, 155-70.degree./0.1-0.15, 62; (CH<sub>2</sub>)<sub>3</sub>, Cl, 155-62.degree./0.06, 73; (CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>, OH, 191-204.degree./0.08-0.18, 80.7; (CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>, Cl, 155-65.degree./0.25, 50; (CH<sub>2</sub>)<sub>4</sub>, OH, 185-240.degree./0.2, 74.9; (CH<sub>2</sub>)<sub>4</sub>, Cl, 160-95.degree./0.3, 53.5. A mixt. of 23 g. VIIb, 19.2 g. IV, and 31.8 g. anhyd. Na<sub>2</sub>CO<sub>3</sub>, in 400 ml. C<sub>6</sub>H<sub>6</sub> was refluxed 15 hrs., and filtered, and the filtrate fractionally distd. to give III. The following I were similarly prep'd. (n, A, R, b.p./mm., % yield, and m.p. of HCl salt given); 4, (CH<sub>2</sub>)<sub>3</sub>, p-MeO, 220-45.degree./0.1, 65, 225.5-6.5.degree. (decompn.); 4, (CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>, o-MeO, 240-60.degree./0.2, 20, 206.5-8.5.degree.; 4, (CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>, H, 190-260.degree./0.25-0.35, 86, 155-7.degree.; 4, (CH<sub>2</sub>)<sub>3</sub>, m-Me, 160-85.degree./0.5-0.1, 92, 240.5-2.5.degree. (decompn.); 4, (CH<sub>2</sub>)<sub>3</sub>, H, 240-60.degree./0.2, 69, 217.5-18.5.degree.; 4, (CH<sub>2</sub>)<sub>4</sub>, o-F, -, 158-90.degree.; 4, (CH<sub>2</sub>)<sub>4</sub>, o-MeSO<sub>2</sub>NH<sub>2</sub>, -, 73.5, 263.5-4.5.degree.; 4, (CH<sub>2</sub>)<sub>4</sub>, o-NO<sub>2</sub>, 150-80.degree./0.1, 26.8, -. I contg. multiple substituents in the Ph ring were similarly prep'd. and were tabulated but not characterized. A mixt. of 15.28 g. II, 200 ml. C<sub>6</sub>H<sub>5</sub>N, and 5.0 g.

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 propargylamine was refluxed overnight in the absence of moisture and fractionally distd. in vacuo (b0.15 129-45.degree.) to give crude 8-propargyl-8-azaspiro[4.5]decane-7,9-dione (VIII) contaminated with II. A mixt. of 6.0 g. VIII, 2.4 g. 37% aq. HCHO, a few crystals of CuCl (catalyst), 1.78 g. AcOH, 2.9 g. distd. H<sub>2</sub>O, and 4.8 g. 1-phenylpiperazine was heated under N<sub>2</sub> on a water bath at 40.degree. 7 hrs., extd. with 3 times 75 ml. CHCl<sub>3</sub>, and worked up in the usual manner, and the product converted to the HCl salt to give 6.5 g. 8-[4-(4-phenyl-1-piperazinyl)-2-butynyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 173-4.degree. (EtOH). Similarly prep'd. was 8-[4-(*o*-methoxyphenyl)-1-piperazinyl]-2-butynyl-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. IT 21090-08-42 21102-92-1P 21102-93-2P 21102-94-3P 21102-95-4P 21102-98-7P 21102-99-8P 21103-14-0P 21103-15-1P 21103-16-2P 21103-17-3P 21103-20-8P 21103-21-9P 21103-23-1P 21103-24-2P RL SPN (Synthetic preparation), PREP (Preparation) (prep'n. of)  
 RN 21090-07-3 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

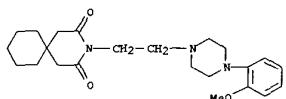


RN 21090-08-4 CAPLUS  
 1,1-Cyclopentanediacetamide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

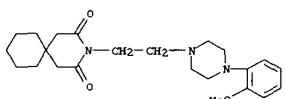


● HCl

RN 21102-92-1 CAPLUS  
 CN 1,1-Cyclohexanediacetimide,  
 N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-  
 (8CI) (CA INDEX NAME)

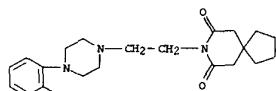


RN 21102-93-2 CAPLUS  
 CN 1,1-Cyclohexanediacetimide,  
 N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-  
 , hydrochloride (8CI) (CA INDEX NAME)

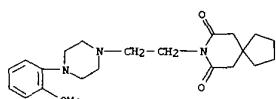


● x HCl

RN 21102-94-3 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-  
 piperazinyl]ethyl]- (8CI) (CA INDEX NAME)

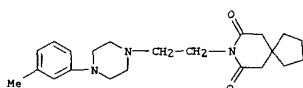


RN 21102-95-4 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-  
 piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)

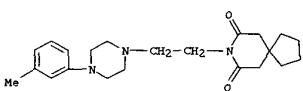


●2 HCl

RN 21102-98-7 CAPLUS  
 CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-  
 (8CI) (CA INDEX NAME)

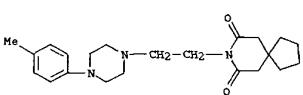


RN 21102-99-8 CAPLUS  
 CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-,  
 monohydrochloride (8CI) (CA INDEX NAME)

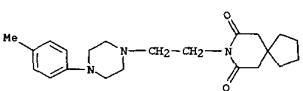


● HCl

RN 21103-14-0 CAPLUS  
 CN 1,1-Cyclopentanediacetimide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-  
 (8CI) (CA INDEX NAME)

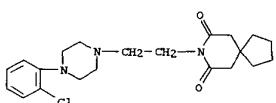


RN 21103-15-1 CAPLUS  
 CN 1,1-Cyclopentanediacetimide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-,  
 dihydrochloride (8CI) (CA INDEX NAME)

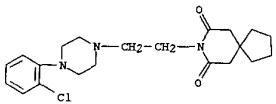


●2 HCl

RN 21103-16-2 CAPLUS  
 CN 1,1-Cyclopentanediacetimide,  
 N-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]-  
 (8CI) (CA INDEX NAME)

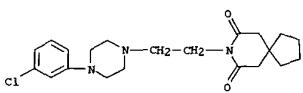


RN 21103-17-3 CAPLUS  
 CN 1,1-Cyclopentanediacetimide,  
 N-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]-  
 , monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 21103-20-9 CAPLUS  
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-  
 piperazinyl]ethyl]- (8CI) (CA INDEX NAME)



RN 21103-21-9 CAPLUS  
 CN 1,1-Cyclopentanediacetimide,  
 N-[2-[4-(m-chlorophenyl)-1-piperazinyl]ethyl]-  
 , monohydrochloride (8CI) (CA INDEX NAME)

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1972:443062 CAPLUS  
DOCUMENT NUMBER: 77:43062  
TITLE: **Psychosedative** agents. 2. 8-(4-Substituted  
1-piperazinylalkyl)-8-azaspiro[4.5]decane-7,9-diones  
AUTHOR(S): Wu, Yao-Hua; Rayburn, J. W.; Allen, L. E.; Ferguson,  
H. C.; Kissel, J. W.  
CORPORATE SOURCE: Dep. Chem. Res., Mead Johnson Res. Cent., Evansville,  
Indiana, USA  
SOURCE: J. Med. Chem. (1972), 15(5), 477-9  
CODEN: JMCMAR  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Several of the title compds. synthesized had greater potency and  
selectivity as tranquilizers than chlorpromazine [50-53-3]. Thus,  
2-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-  
dione (I) [33386-08-2] had an ED50 for complete suppression of  
conditioned avoidance response of 4.3 mg/kg i.p. in rats; 19.6 times this dose was  
required for complete suppression of the unconditioned escape response.  
Corresponding data for the 2-pyridyl analog and chlorpromazine were 2.8  
and 4.8 mg/kg, and 12.1 and 10.2 times, resp. I produced much less  
sedation than chlorpromazine, had very little .alpha.-**adrenergic**  
blocking activity in vivo and in vitro, and had an LD50 of 146 mg/kg i.p.  
in mice. The incidence of catalepsy induced by I in monkeys was similar  
to that with chlorpromazine. To synthesize I,  
N-(2-pyrimidinyl)piperazine  
was prep'd. from piperazine and 2-chloropyrimidine by nucleophilic  
aromatic substitution, reacted with .omega.-chloropropionitrile, reduced with  
LiAlH4 or Raney Ni-H2 to 1-(.omega.-aminobutyl)-4-(2-  
pyrimidinyl)piperazine, and reacted with the spiro compd.  
cyclopentane-1,1-diacetic acid anhydride.

L9 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1997:260493 CAPLUS  
DOCUMENT NUMBER: 126:312328  
TITLE: Recent advances in the identification of .  
alpha.1- and .alpha.2 adrenoceptor  
subtypes: therapeutic implications  
AUTHOR(S): Hieble, J. Paul; Rufolo, Robert R., Jr.  
CORPORATE SOURCE: Div. Pharm. Sci., SmithKline Beecham Pharm., King of  
Prussia, PA, 19406, USA  
SOURCE: Expert Opinion on Investigational Drugs (1997), 6(4),  
367-387  
CODEN: EOIDER; ISSN: 0967-8298  
PUBLISHER: Ashley Publications  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review, with 166 refs. The cloning of multiple subtypes of both .alpha.1- and .alpha.2-adrenoceptors has renewed interest in the therapeutic application of agents interacting with these receptors. Effort has primarily been directed towards the design of uroselective .alpha.1-adrenoceptor antagonists for the treatment of benign prostatic hyperplasia (BPH). Evidence is accumulating for the involvement of a novel .alpha.1L-adrenoceptor, designated as .alpha.1L-adrenoceptor, in .alpha.1L-adrenoceptor-mediated smooth muscle contraction in prostatic and other urogenital tissues. While several antagonists showing a high degree of uroselectivity in animal models have been identified, their clinical superiority over the currently available .alpha.1-adrenoceptor antagonists has not yet been demonstrated. It is possible that the interaction with .alpha.1L-adrenoceptors, as yet uncharacterized subtypes, at nonprostatic sites contributes to the therapeutic activity of this drug class in BPH. The .alpha.1L-adrenoceptor subtypes involved in the control of vascular tone are currently being evaluated, and the profile of interaction with the various .alpha.1L-adrenoceptor subtypes may play a key role in the efficacy of cardiovascular drugs such as carvedilol. .alpha.2-Adrenoceptor agonists are now being employed for a variety of therapeutic applications, most involving actions on receptors with the central nervous system (CNS). These agents are useful in the treatment of hypertension, glaucoma, opiate withdrawal and attention deficit hyperactivity disorder (ADHD), and as analgesics and adjuncts to general anesthesia. While subtype selectivity has not yet been applied to the design of new .alpha.2-adrenoceptor agonists for these applications, recent gene mutation/knock-out experiments have identified the .alpha.2-subtypes involved in some of these actions, and optimization of a therapeutic profile may be possible. Furthermore, the design of agents combining affinities for multiple adrenoceptor subtypes, or the combination of a specific adrenoceptor affinity profile with another pharmacological action, may offer advantages over molecules selective for an individual adrenoceptor subtype.

L9 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1997:65995 CAPLUS  
DOCUMENT NUMBER: 126:113272  
TITLE: Role of prostaglandins in the stimulation of the hypothalamic-pituitary-adrenal axis by **adrenergic** and neurohormone systems  
AUTHOR(S): Bugajski, J.  
CORPORATE SOURCE: Institute Pharmacology, Polish Academy Sciences, Krakow, Pol.  
SOURCE: Journal of Physiology and Pharmacology (1996), 47(4), 559-575  
PUBLISHER: Polish Physiological Society  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 78 refs. Role of prostaglandins (PGs) in the activation of the hypothalamic-pituitary-adrenal (HPA) axis by the **adrenergic** agonists, ACTH-releasing hormone (CRH) and vasopressin (VP) in rats under basal and social stress conditions was investigated. Systemic or intracerebroventricular (icv) pretreatment with indomethacin powerfully reduced the corticosterone response to icv phenylephrine, an **alpha.1-receptor** agonist, significantly diminished the response to clonidine, an **alpha.2-receptor** agonist, but did not alter the response to isoproterenol, a **beta.-adrenergic** agonist. Consequently, indomethacin considerably reduced the corticosterone response to noradrenaline, an **alpha.1-** and **alpha.2-adrenergic** agonist, but did not change the response to adrenaline, a predominant **beta.-adrenergic** agonist. Thus, prostaglandins considerably mediate the HPA activity stimulated via central **alpha.1**-and **alpha.2**-but not **beta.-adrenergic receptors**. Social crowding stress for 3 days did not affect the corticosterone response to i.p. or icv CRH, but drastically reduced the response to VP. In stressed rats indomethacin did not alter the corticosterone response to CRH but significantly further impaired the diminished by stress corticosterone response to VP. Neither social stress nor endogenous prostaglandins affected the responsiveness of the CRH system. By contrast, both social stress and prostaglandins considerably diminished the HPA response to VP. The above results indicate that both these neurohormone systems have a distinct mode of adaptation and interaction with PG systems during social stress. Interleukins, particularly IL-1.**beta.** and IL-6, activate the HPA axis. Most immunol. stimuli and interleukins also activate both the central and the peripheral noradrenergic systems. Activation of the HPA axis *in vivo* depends on the secretion of CRH, an intact pituitary and the ventral **adrenergic** bundle innervating the hypothalamic paraventricular nucleus. Interleukins may cross the blood-brain-barrier or be produced in the CNS to stimulate their **receptors** in brain structures involved in the regulation of the HPA axis.

L9 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1992:400953 CAPLUS  
DOCUMENT NUMBER: 117:953  
TITLE: Electrophysiological consequences of activation of  
adrenoceptors in the CNS  
AUTHOR(S): McCormick, David A.  
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, USA  
SOURCE: Adrenoceptors: Struct., Mech., Funct., [Proc.  
Manchester Symp. Pharmacol. Adrenoceptors], 3rd  
(1991)  
, Meeting Date 1990, 159-69. Editor(s): Szabadi,  
Elmer; Bradshaw, Christopher M. Birkhaeuser: Basel,  
Switz.  
CODEN: 57QSAA  
DOCUMENT TYPE: Conference; General Review  
LANGUAGE: English  
AB A **review**, with 30 refs., on the electrophysiolog. consequences of  
activation of .alpha.1-, .alpha.2-, and  
.beta.-adrenoceptors in the central nervous system (**CNS**).

L9 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1983:516128 CAPLUS  
DOCUMENT NUMBER: 99:116128  
TITLE: The physiological role of .alpha.  
. -adrenoceptors in the CNS: new concepts  
from single-cell studies  
AUTHOR(S): Aghajanian, G. K.; Rogawski, M. A.  
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06508, USA  
SOURCE: Trends Pharmacol. Sci. (1983), 4(7), 315-17  
CODEN: TPHSDY; ISSN: 0165-6147  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review with 10 refs., on the synaptic localization and  
functional classification of .alpha.1- and .alpha.2-  
**adrenergic receptors** in the central nervous system.